



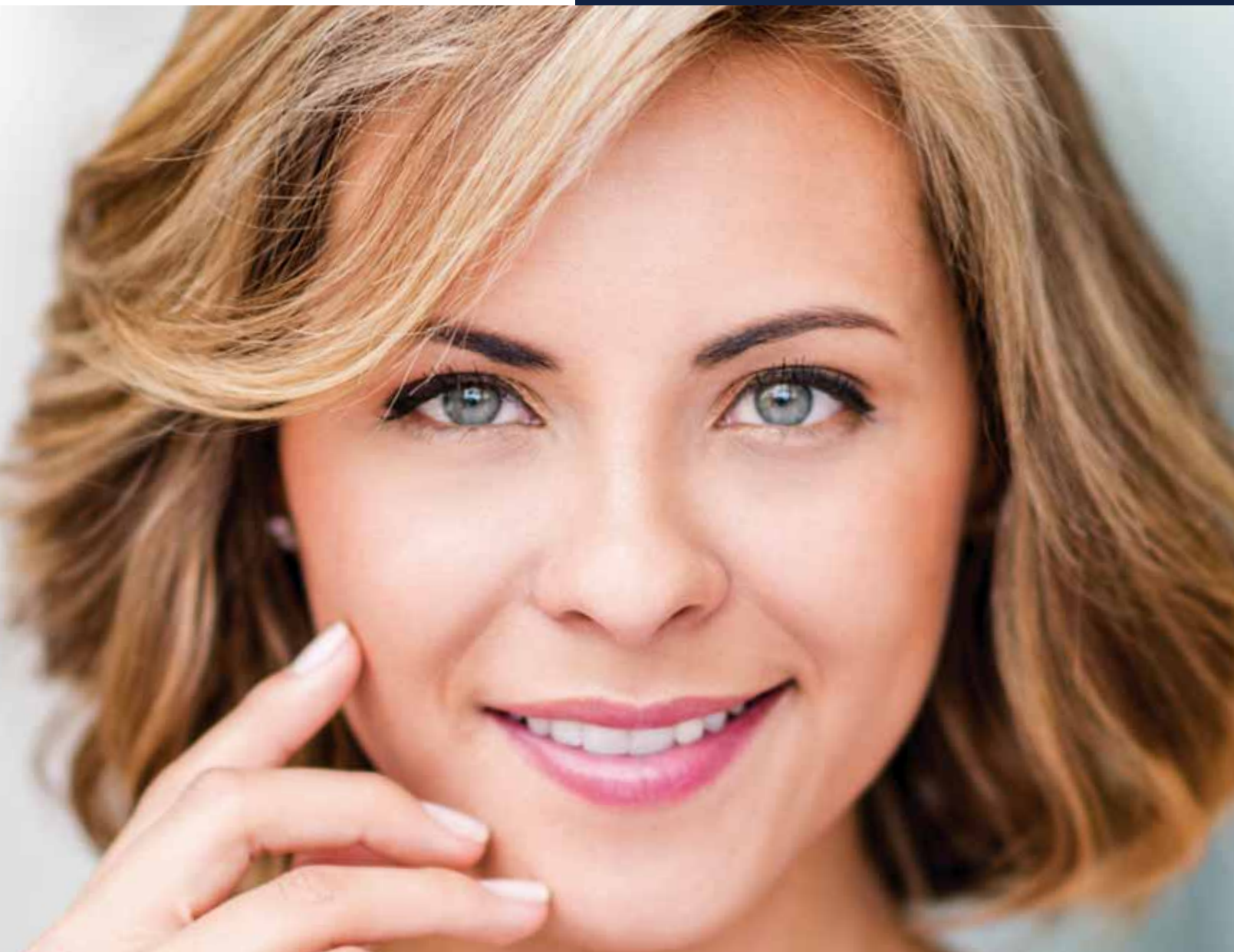
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June 2021

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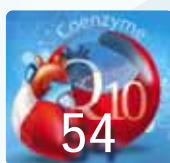
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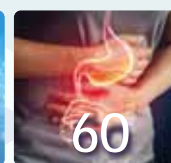
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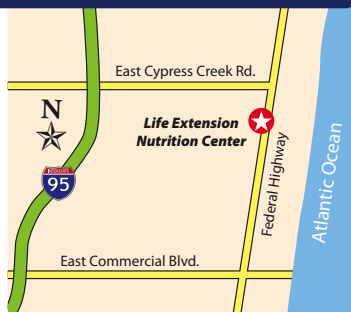


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# Outbreak of Metastatic Prostate Cancer



WILLIAM FALOON

**Prostate cancer** is the second leading cause of cancer **death** in American men.<sup>1</sup>

It is estimated that over **34,000** deaths will occur from **metastatic prostate cancer** in **2021**.<sup>1</sup>

Low-cost **PSA blood testing** is one of our most valuable tools for detecting prostate cancer when it is still in its *early* curable stages.<sup>2</sup>

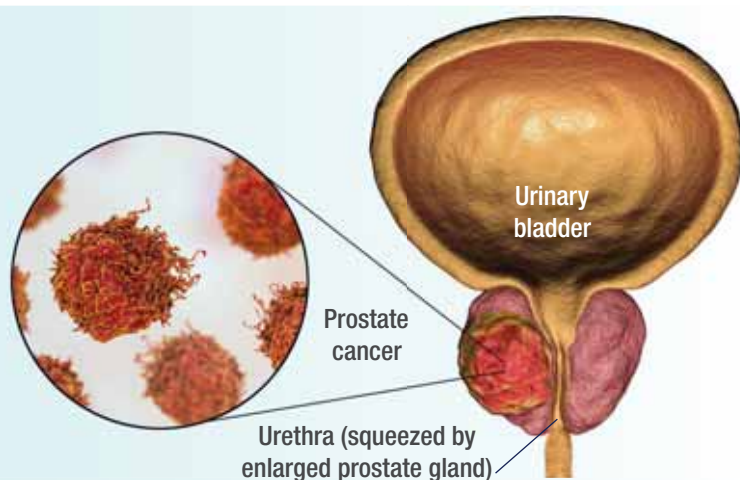
## Our Dire Prediction Transforms into Lethal Reality

**The United States Preventive Services Task Force (USPSTF)** is a government-funded group that claims:

*"to improve the health of all Americans by making evidence-based recommendations about clinical preventive services."*

In **2012** the **USPSTF** made a **misguided** recommendation that compelled me to write an editorial describing the **USPSTF** as a:

*"Federal Death Panel"<sup>3</sup>*



In **2008**, the **USPSTF** recommended that men over **age 75** not have their blood routinely screened for **PSA**.<sup>4</sup>

In **2012**, the **USPSTF** recommended against routine **PSA screening** for all men 50 years of age and older.<sup>5</sup>

The initial effect of the **USPSTF's** recommendations were declines in prostate cancer diagnosis. Everyone agreed this would happen because if the number of "**PSA tests**" go down, so do new cases... at least in the beginning.

Tragically, too many men who followed the **USPSTF** guidelines to not test their **PSA** are now facing advanced-stage prostate cancers.

As of **2016**, a total of **11,387 more** American men were diagnosed with **metastatic prostate cancer** compared to **2008** levels, when **PSA blood test** prevalence was robust.<sup>6</sup>

Few of these **metastatic prostate cancer** patients will be **cured**.<sup>7</sup> Some are kept alive by grueling **chemotherapy, radiation** and **hormone-ablation** regimens, including **castration** in some cases.

Had the **USPSTF** not swept prostate cancer "**under the rug**" by recommending against **PSA screening**, thousands of lives could have been saved and an enormous amount of human suffering avoided.

As surging numbers of men succumb to advanced disease and harsh treatments, our dire prediction **8-12 years** ago has been tragically **vindicated**.

This is of little value to those not able to recognize that the **USPSTF** was not acting on behalf of **humanity**.

**PSA** stands for: **prostate-specific antigen**.

When **PSA** blood levels increase above **1.0-2.0 ng/mL** it may indicate a very *early-stage* **cancer** that is **reversible** in some cases by making healthy dietary choices.<sup>8-10</sup>

PSA is not just a potential prostate cancer **marker**.

Prostate cells can emit PSA to break down healthy prostate tissues and help malignant cells invade tissues.<sup>11,12</sup> This can enable **malignant** prostate cells to penetrate the prostate capsule and spread to soft tissue, regional lymph nodes and eventually bones.

A **PSA** reading over **1.0 ng/mL** indicates that prostate health is in jeopardy.

One study, published in the *New England Journal of Medicine*, showed that **17%** of the men with PSA levels between **1.1 to 2.0 ng/mL** had **prostate cancer**.<sup>13</sup>

PSA increases at different rates in different conditions. In **benign prostatic hypertrophy (BPH)** there is usually a slow PSA increase over time. In **prostate cancer**, PSA levels can double over a relatively short period.<sup>14</sup>

## How to Lower PSA Levels

PSA levels increase with age, but there are **proven** ways to reduce it.

These methods range from choosing healthier **diets/lifestyles** to taking drugs like **Avodart®** now sold as a generic called **dutasteride**. The typical **dutasteride** dose is **0.5 mg/day** to improve urinary flow.<sup>15</sup>

Men who use drugs like **dutasteride** or **finasteride** shrink their prostate gland size about **25%** and reduce their **prostate cancer** risk by around **25%**.<sup>16-18</sup>

A minority of men complain about **sexual** side effects, while others are happy with improved head **hair** growth.

I often suggest that men with rising **PSA levels** who don't want to use **dutasteride** make **dietary** changes that may accomplish similar benefits.

## Advent of PSA Blood Testing

**PSA blood tests** became available around year **1990** and American men were quick to utilize them. In the **United Kingdom**, PSA testing was much less common.

This enabled researchers to study trends in **prostate cancer mortality** in the **United States** versus the **UK** spanning years **1975 to 2004**.<sup>19</sup> A comparative analysis was done to assess whether more **PSA screening** resulted in fewer prostate cancer **deaths**.

This study found that **prostate cancer mortality** peaked in the *early 1990s* at almost identical rates in both the USA and UK.



Starting after **1994**, however, age-adjusted prostate cancer **death rates** in the **United States** declined **four times more** compared to those in the **United Kingdom** after **1992**.

Both countries saw declines in prostate cancer deaths because of improved treatments and overall earlier detection, but the decline was **four times greater** in the **United States**. The best available explanation for this difference is the earlier **PSA detection** and better treatment options available in the United States.

The decline in **prostate cancer mortality** in the **United States** was greatest and most sustained in men aged **75** or older.

These findings were published in *The Lancet Oncology* with the following interpretations:<sup>19</sup>

*“The striking decline in prostate cancer mortality in the USA compared with the UK in 1994–2004 coincided with much higher uptake of PSA screening in the USA.”*

These data published in **May 2008** showed the greatest death rate decline in response to **PSA testing** occurred in men over **age 75**.

Despite these findings, the **United States Preventive Services Task Force (USPSTF)** issued a recommendation in **August 2008** (widely disseminated by the media) that older men should not undergo **PSA screening**.



This specific **USPSTF** recommendation of **August 2008** was:<sup>20</sup>

*"Do not screen for prostate cancer in men age 75 years or older."*

### Fighting Back Against USPSTF Guidelines

In **2012**, the **USPSTF** went a step further and recommended against routine **PSA screening** for all men ages 50 and older.<sup>5</sup>

This led to an uproar among various medical specialists who argued for and against routine **PSA screening**.

**Life Extension®** led a charge against these egregiously misguided **USPSTF** anti-PSA-testing recommendations.

We persuaded large numbers of men to continue having annual **PSA blood tests** in order to detect prostate malignancies in *early* stages when they are curable using minimally invasive therapies like high-resolution image-guided **cryo-ablation**.

### Partial Capitulation

As scientific evidence mounted against the **USPSTF's** position on **PSA screening**, a major concession was made.

In 2018 the **United States Preventive Services Task Force** (USPSTF) backtracked on its 2012 recommendation against PSA screening. Their new suggestion is that men aged 55–69 should make an

individual decision about routine screening in consultation with their physician.<sup>21</sup>

While this represents a partial capitulation, we vehemently disagree that early diagnosis of prostate cancer should be limited to men aged **55–69**.

Prostate cancer risk begins around age 40,<sup>22</sup> and this is when men should have their first PSA blood test.

We at **Life Extension®** don't write off men over age 69, and we urge these men to have annual PSA blood tests to ascertain prostate cancer risk and take steps to reverse the course of early-stage disease using nutritional and drug interventions.

### Diagnoses Decline but then Head Higher

On **May 23, 2020**, a study was published that evaluated American men who developed **regional** (outside the prostate capsule) and **metastatic** prostate cancers since **PSA screening** was first discouraged in **2008**.<sup>6</sup>

As expected, rates of newly diagnosed prostate cancers declined as fewer men underwent **PSA blood tests**. But avoiding a PSA test does not make the disease disappear. It only **delays** the eventual diagnosis to a time when the prostate cancers are more advanced and often incurable.

For example, this study found that for the years **2007** to **2016**, the incidence of local-stage, non-advanced prostate cancer decreased by **6.4%** per year in men ages 50 to 74, and by **10.7%** per year in men ages 75 years and beyond.<sup>6</sup>



These decreases in early-stage disease reflected fewer PSA tests being performed, which meant fewer men were diagnosed in asymptomatic stages when cure rates are very high.

For **regional-stage** prostate cancer, where the tumor extends beyond the prostate capsule, but is contained in the pelvic genital-urinary region, incidence rates surged **11.1%** per year **higher** from **2012-2016** after stable rates from **2005-2012**.<sup>6</sup>

For distant-stage, advanced prostate cancer, incidence increased from **2010-2016** by **5.0% per year** after declining by **0.9%** per year from **2005-2010**.<sup>6</sup>

This means there were increased rates of **advanced** (regional- and distant-stage disease) **prostate cancers** in the years (**2010-2016**) after **PSA screening** began plummeting.

A major factor likely responsible for this increased incidence per year from **2010-2016** in regional- and distant- stage disease was the USPSTF guidelines recommending against routine **PSA screening**.

## How Many Men Impacted By Year 2016?

The researchers looked at how many excess cases of metastatic prostate cancer occurred from **2009** through **2016** and compared them to the historically low **2008** rate (before **USPSTF** advised against **PSA screening**).<sup>6</sup>

A total of **11,387 more** men aged 50 or greater were diagnosed with distant-stage (**metastatic**) prostate cancers from **2009-2016** in the U.S. than would have been, had the incidence of advanced-stage/metastatic disease remained at **2008** levels.<sup>6</sup>

The researchers commented that in **2016** alone, the last year of the analysis, there were **3,590 additional** men living with advanced-stage **metastatic** prostate cancer because of the change in incidence since **2008** (when **PSA screening** was widespread).

## Declining Rates of PSA Testing

The USPSTF's attack on PSA blood testing had a huge impact on reducing the number of men over age 50 who underwent **PSA screenings**.

## What if Your PSA Blood Level is Elevated?

The "normal" reference range for **PSA** is **0-4 ng/mL**.

The optimal **PSA** blood level is **1.0 ng/mL** and lower for healthy men.

When **PSA** becomes elevated above **1.0-2.0 ng/mL**, this indicates activity in the prostate gland that may relate to **inflammation, benign growth, and/or cancer**.

Unlike typical cancers, some prostate malignancies appear **reversible**.

Nutrients like **curcumin**,<sup>26,27</sup> **boron**,<sup>28,29</sup> and **vitamin D**<sup>30-33</sup> have been shown to support prostate health and facilitate **PSA** reduction.

Drugs like **finasteride** and **dutasteride** can cut **PSA** by **50%**.<sup>34,35</sup> This is more than just a number-reducing effect. Men taking these drugs reduce their **prostate cancer** risk by about **25%**.<sup>16-18</sup>

When **PSA** levels are above **1.0-2.0 ng/mL**, this can be an early warning that a problem is

developing in the prostate gland. After dietary, nutrient and/or drug therapies are initiated, the **PSA** should be retested in the next three to six months to ensure the changes are resulting in a reduced **PSA** level.

Annual (or twice yearly) **PSA blood tests** thereafter enable an aging man and his physician to monitor the status of his prostate gland, both from a quality-of-life standpoint as it relates to BPH and to catch a malignancy in its early stages when cure rates are virtually **100%**.

New minimally invasive techniques can now be done on an outpatient basis. These include enhanced imagery-guided **cryo-ablation** or **laser** therapies that seek to destroy *only* the **malignant** portion of the prostate gland.

This is a vast improvement over conventional methods involving **radical prostatectomy** (major surgery) or **radiation** that damages surrounding healthy tissues.



## Table 1. Timeline for PSA Testing

- 1990s:** PSA blood tests become widely available in U.S.
- 2008:** PSA blood testing peaks in U.S.
- 2008:** Study shows PSA testing reduces prostate cancer mortality.
- 2008:** USPSTF urges men over 75 years to avoid PSA screening.
- 2012:** USPSTF urges all men to avoid PSA screening.
- 2013:** Life Extension® alleges USPSTF functions as a “death panel.”
- 2018:** USPSTF says men aged 55-69 may consider PSA screening.
- 2020:** Report reveals relative surge in advanced prostate cancer since 2008.

According to national self-reported survey data, routine **PSA testing** rates among men age 50 years and over were at **40.6%** in **2008**. That meant that **40%** of American men over age 50 had their blood tested to check **PSA** levels.<sup>23,24</sup>

This percent of men aged 50 and over having routine PSA tests dropped to **38.3%** in **2010** and then to **31.5%** in **2013** and remained unchanged in **2015**.<sup>23,24</sup>

Similar declines in PSA testing have been reported on Medicare claims data.<sup>25</sup>

This decline in **PSA testing** correlates with the surge in **regional-** and **advanced-stage (metastatic)** incidence for prostate malignancies over this time period.

## How Many Men Affected Since Year 2016?

Prostate cancer is often an insidious, slow-growing disease without outward side effects.

The first symptom of metastatic disease can be bone pain (back or pelvic areas) as prostate cancer cells infiltrate into bone and accelerate its breakdown.

Bony metastasis is often termed stage 4 disease. It can be treated with hormone ablation, radiation and chemotherapy drugs to enable a man to live for many years—but while enduring chronic pain and disability inflicted by the malignant cells, the toxic drugs/radiation, and the deprivation of testosterone.

Testosterone deprivation is associated with significant mental and physical health issues such as depression, aggravation of cardiovascular disease, acceleration of frailty, and muscle wasting.

As new data sets emerge, we will learn how many more men who avoided PSA screening are afflicted with advanced malignancies.

## Impact of Misguided Recommendations Not Yet Known

I continue to predict that the decline in **PSA screening** will result in more men being diagnosed with advanced prostate malignancies.

Compare the tragedy of delayed diagnosis to far gentler procedures like precise imaging-guided **cryo-ablation** that is often **curative** when the disease is caught in localized (early) stages.

I am gratified to those who stood up to the **USPSTF** and unwarranted media attacks on **PSA screening** so that at least **30%** of men over age 50 today are likely having regular **PSA blood tests**.

There are historic examples of effective procedures falling out of favor with a corresponding increase in the numbers of people who needlessly suffer and die.

One such example is **scurvy**, the disease that sickened and killed millions, long after a citrus cure was discovered. (See Table 2 below for a brief chronology.)

## Table 2. How Scurvy Relates to PSA Test Debates

- 1497:** Citrus shown to cure scurvy.
- 1747:** James Lind proves citrus cures scurvy.
- 1799:** Britain mandates sailors ingest citrus.
- 1870:** Citrus cure officially discredited.
- 1911:** Dr. Robert Scott loses crew to scurvy.
- 1932:** Vitamin C proven to cure scurvy.

## Thousands of Deaths After Cure is Discovered

Most male readers of **Life Extension®** magazine screen for **PSA** and make adjustments if levels are higher than optimal.

As you can see on the next page, PSA testing is included in the popular **Male Blood Test Panel** that many of our readers utilize each year.

For longer life,



William Faloan, Co-Founder

**Life Extension Foundation Buyers Club, Inc.**

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## MALE PANEL

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**NEW** Ferritin (measure of iron status)

Serum Magnesium

**Kidney function tests:** creatinine, BUN, uric acid, BUN/creatinine ratio

**Liver function tests:** AST, ALT, LDH, GGT, bilirubin, alkaline phosphatase

**Blood minerals:** calcium, potassium, phosphorus, sodium, chloride, iron

**Blood proteins:** albumin, globulin, total protein, albumin/globulin ratio

### CARDIAC MARKERS

Apolipoprotein B (ApoB)

Homocysteine

C-Reactive Protein (high sensitivity)

### LIPID PROFILE

Total Cholesterol

LDL (low-density lipoprotein)

HDL (high-density lipoprotein)

Triglycerides

### COMPLETE BLOOD COUNT (CBC)

**Red Blood Cell count including:** hemoglobin, hematocrit, MCV, MCH, MCHC, RDW

**White Blood Cell count including:** lymphocytes, monocytes, eosinophils, neutrophils, basophils

Platelet count

### CANCER MARKER

PSA (Prostate Specific Antigen)

### HORMONES

Free and Total Testosterone

DHEA-S

Estradiol (an estrogen)

TSH (thyroid function)

Vitamin D

## FEMALE PANEL

### METABOLIC PROFILE

Glucose

Insulin

Hemoglobin A1c

**NEW** Ferritin (measure of iron status)

Serum Magnesium

**Kidney function tests:** creatinine, BUN, uric acid, BUN/creatinine ratio

**Liver function tests:** AST, ALT, LDH, GGT, bilirubin, alkaline phosphatase

**Blood minerals:** calcium, potassium, phosphorus, sodium, chloride, iron

**Blood proteins:** albumin, globulin, total protein, albumin/globulin ratio

### CARDIAC MARKERS

Apolipoprotein B (ApoB)

Homocysteine

C-Reactive Protein (high sensitivity)

### LIPID PROFILE

Total Cholesterol

LDL (low-density lipoprotein)

HDL (high-density lipoprotein)

Triglycerides

### COMPLETE BLOOD COUNT (CBC)

**Red Blood Cell count including:** hemoglobin, hematocrit, MCV, MCH, MCHC, RDW

**White Blood Cell count including:** lymphocytes, monocytes, eosinophils, neutrophils, basophils

Platelet count

### HORMONES

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Estradiol (an estrogen)

Free and Total Testosterone

DHEA-S

TSH (thyroid function)

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# In the News



## Low Testosterone Linked to Higher Mortality Rate

Men with low levels of **testosterone** have a greater mortality rate from any cause, compared with those who had higher levels, a study published in the *Journal of Clinical Endocrinology & Metabolism* reported.\*

The study included 149,436 men between the ages of 40 and 69, who enrolled in the UK Biobank from 2006 to 2010. Blood samples collected at enrollment were analyzed for serum testosterone. The subjects were followed from recruitment through April 2020.

During the follow-up period, 10,053 deaths were documented, including 1,925 from cardiovascular disease and 4,927 from cancer.

Compared to men whose testosterone levels were among the top **20%** of participants, those whose testosterone levels were among the lowest **20%** had a **14%** greater risk of dying from any cause and a **20%** greater risk of dying from cancer during the follow-up period.

**Editor's Note:** "Serum testosterone concentrations decline with age, while serum sex hormone-binding globulin (SHBG) concentrations increase," the authors stated. They concluded that, "Lower serum testosterone is independently associated with higher all-cause and cancer-related, but not CVD-related, mortality in middle-aged to older men. Lower SHBG is independently associated with lower all-cause, CVD-related, and cancer-related mortality."

\* *J Clin Endocrinol Metab.* 2021 Feb;106(2):e625-637.

## Healthy Diet Connected to Good Gut Microbes, Lower Disease Risk

In the largest, most detailed study of its kind, researchers found that diets rich in plant-based foods encourage the presence of gut microbes that are connected to a lower risk of diseases like heart disease and type II diabetes, according to an article in *Nature Medicine*.\*

Researchers performed deep metagenomic sequencing of 1,203 gut microbiomes from 1,098 people enrolled in the PREDICT 1 study, which included long-term diet information, plus fasting, and same-meal postprandial cardiometabolic blood-marker measurements.

The researchers found significant associations between gut microbes and specific nutrients, foods, and dietary practices. They identified strong microbiome-based markers of obesity, cardiovascular disease, and impaired glucose tolerance.

**Editor's Note:** People who consumed healthy, plant-based foods were more likely to have high levels of good gut bacteria, while people consuming diets with more processed foods were more likely to have bad gut bacteria, the authors stated.

\* *Nat Med.* Feb;27(2):321-332.







## CoQ10 Provides Relief from Fatigue

Results from a study published in *Nutrients* reveal a benefit for supplementing with coenzyme Q10 (CoQ10) against mild, daily fatigue.\*

The study enrolled men and women aged 20 to 64 who experienced fatigue during their daily lives for at least one month and for no longer than six months.

Twenty participants were given **100 mg** of the form of CoQ10 known as **ubiquinone**, 22 participants received **150 mg** of the **ubiquinol** form of CoQ10 and 20 received a **placebo** daily for 12 weeks.

At the end of the study levels of serum ubiquinol, which is the reduced form of CoQ10, were significantly *higher* in the group that received ubiquinol compared to levels measured in those who received a placebo.

Subjective levels of sleepiness or fatigue following cognitive tasks significantly improved in both **CoQ10** groups compared with the placebo group.

**Editor's Note:** Participants who received **ubiquinol** additionally experienced improvement in subjective relaxation following the completion of cognitive tasks, sleepiness before and after tasks, task motivation and serum oxidative stress levels, compared to the placebo group.

\* *Nutrients*. 2020 Jun 2;12(6):E1640.

## Fewer Adverse Effects After Heart Attack in Those with Greater Omega-3 Intake

An association was found between increased intake of omega-3 fatty acids and a lower risk of clinical adverse effects in patients who experienced a heart attack, the *Journal of the American College of Cardiology* reported.\*

The study included 944 patients treated for heart attack with coronary artery stents and/or balloon angioplasty.

Blood samples were analyzed for levels of the omega-3 fatty acids, EPA (obtained from fish), and ALA (alpha linolenic acid), a precursor to EPA/DHA found in plants.

Compared to subjects who had lower levels of EPA at the time of their heart attacks, those who had higher levels had significantly *reduced* risks of experiencing major adverse cardiovascular events and hospital readmission for cardiovascular causes during the three-year follow-up period. Higher levels of ALA were associated with a significantly reduced risk of mortality from all causes during follow-up.

**Editor's Note:** Consumption of foods rich in these fatty acids might improve the prognosis of heart attack patients, the authors concluded.

\* *J Am Coll Cardiol.* 2020 Nov 3;76(18):2089-2097.





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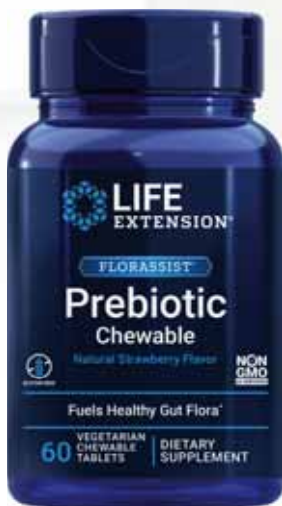
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1. *Front Microbiol.* 2016;7:1204.
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WOOD BOX





# Rejuvenate Skin from Within

BY MICHAEL DOWNEY

Our **skin** contains natural **moisturizing** oils known as **ceramides**.

When we're young, they keep skin firm, moist, and wrinkle-free.

But with age, **ceramide production** *declines*, resulting in dry, sagging skin and wrinkling.<sup>1,2</sup>

Pollution and exposure to ultraviolet (UV) radiation accelerate this skin aging process.<sup>3</sup>

Researchers have found ways to prevent and *reverse* some of this damage with oral ceramides and herbal extracts.

**Oral ceramides** derived from **rice** are thought to work internally to boost production of ceramides in skin, promoting a more hydrated, youthful appearance.<sup>4,5</sup>

Additionally, researchers have also identified **four herbal extracts** that work together to mitigate skin aging caused by pollution and UV radiation.<sup>6</sup>

In a clinical trial, **96%** of participants taking the herbal extracts had a ***significant reduction in wrinkle depth***.<sup>6</sup>

Taken orally, these nutrients provide a strategic approach to rejuvenate skin and protect against environmental damage.

## Ceramides Stop Skin Aging

**Ceramides** can be thought of like the mortar that holds skin-cell bricks together.

Internal ceramide production declines as we age. This decreases the skin's **moisture barrier**, resulting in thinning, wrinkles, dryness, roughness, and even increased risk of infection.<sup>1,7-12</sup>

Ceramides have been added to some skin creams since the early 1990s. But because **topically** applied ceramides do not reach deeper skin layers, their effects are generally modest.<sup>12,13</sup>

To address this problem, scientists developed plant-derived ceramides—or **phytoceramides**—that can be taken **orally**. These lipids are thought to boost the production of ceramides in the skin.

Researchers have now achieved clinical success by using ceramides from a non-genetically modified rice extract that is **gluten-** and **allergen-free**.<sup>4,5</sup>

Taken orally, these **rice-derived phytoceramides** work from the inside out to hydrate, smooth, and rejuvenate skin all over the body.<sup>4,5</sup>

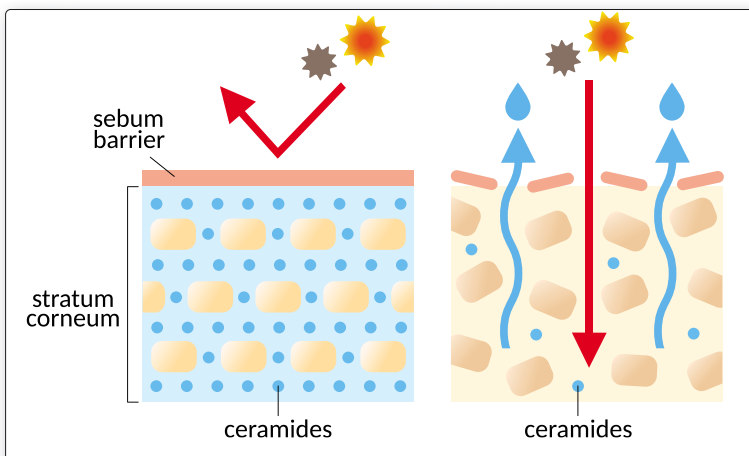
## Herbal Extracts Defend Against External Dangers

Age isn't the only factor driving skin damage.

**External** factors like environmental **pollutants** and **UV radiation** from the sun can degrade the skin's structural integrity, reducing skin firmness and elasticity. That leads to wrinkling and fine lines.<sup>3,14</sup>

In addition to inducing oxidative stress and inflammation, pollutants cause *overexpression* of the protein **aryl hydrocarbon receptor (AhR)**.

**AhR** overactivation increases the expression of genes responsible for oxidative stress, inflammation, immunosuppression, pigmentation, skin cancer, and **premature skin aging**.<sup>6,14</sup>



Researchers have identified four **herbal extracts** that, when taken orally, protect against the damaging effects of pollution and UV exposure as follows:<sup>6</sup>

- Rosemary,
- Olive leaf,
- *Lippia citriodora* (lemon verbena) leaf, and
- *Sophora japonica* (Japanese pagoda tree) leaf.

These extracts have been shown in a **clinical study** to improve skin health and deliver substantial protection against pollutants and UV radiation.<sup>6</sup>

*In vitro* studies show that the extracts inhibit the overactivation of the **AhR receptor** that causes **premature skin aging** and other skin-damaging effects.<sup>6</sup>

The abilities of rice ceramides *and* this herbal blend to block and even reverse skin aging has been validated in human trials.

## Improve Skin Hydration and Barrier Function

Scientists set out to test the effect of **rice-derived ceramides** on **skin barrier function**, the ability to retain moisture and protect against external threats.<sup>4</sup>

They enlisted 123 healthy volunteers with **dry skin**. Every day for 12 weeks, subjects took either **rice extract** providing **ceramides** or a placebo.

Investigators measured water loss that occurs when water passes from the skin's middle layer to the outer layer and evaporates. This test is used as a measure of the skin's barrier function.

In as few as four weeks, subjects taking the rice extract had significant **reduction in water loss** through the skin in nearly *all* body areas, compared to those taking a placebo.<sup>4</sup>

A second clinical trial was conducted on patients (mean age: 30.5 years) with **mild atopic dermatitis**, or **eczema**. This skin disease is characterized by impaired skin barrier function and a reduction in ceramide content, and leads to patches of itchy, dry skin.<sup>5</sup>

Every day for four weeks, the treatment group took a **rice extract** providing **ceramides**.

The **placebo group** had significant water loss over the course of the study, resulting in decreased water content in the outer layer of the skin.<sup>5</sup>



Those supplementing with the rice extract **reduced** their **water loss** by more than **30%** compared to the placebo group. This was seen in visual improvements to skin appearance.<sup>5</sup>

## Reducing Wrinkles

Researchers next tested the effectiveness of the blend of **herbal extracts** in guarding against environmental pollutants.

The combination consisted of:<sup>6</sup>

- Rosemary extract,
- Olive extract,
- *Lippia citriodora* extract, and
- *Sophora japonica* extract.

The researchers enlisted 100 women (aged 35-65 years), **half** of whom had sensitive skin.

The treatment group took **250 mg** of the blend orally for 12 weeks. The researchers measured an exhaustive list of factors, such as skin moisture, radiance, and smoothness to evaluate the overall look and health of skin.<sup>6</sup>

**More than 90%** of treated volunteers had significant improvement in **all** of the measures.<sup>6</sup>

The **herbal blend** smoothed and softened skin, significantly reduced wrinkle depth, and improved skin elasticity and firmness—beginning in **just 15 days**.<sup>6</sup>

Compared to a placebo, after 12 weeks of treatment, the group taking the herbal extracts had:<sup>6</sup>

- A **10-fold** greater decrease in **wrinkle depth**,
- A **3-fold** improvement in skin **moisture**,
- **5 times** the skin brightness or **radiance**,
- **2.5 times** more lightening of **dark spots**,
- A nearly **5-fold** reduction in **water loss**, and
- An **18-fold** greater increase in skin **smoothness**.

These improvements in skin appearance are likely due to the reduction in **water loss**, which indicates a clear improvement in the **skin barrier function**.

A strengthened **barrier function** means pollutants are less able to penetrate to the deeper layers of the skin to cause damage.



## WHAT YOU NEED TO KNOW

### Keep Skin Healthy and Strong

- **Ceramides** are natural oils that keep our skin hydrated and healthy. As we age, our bodies produce fewer ceramides, leading to wrinkles, dryness, and other signs of **skin aging**.
- Scientists have developed **rice-derived ceramides**. Taken *orally*, they have been shown to restore the skin's vital barrier function and youthful skin hydration.
- External factors like environmental **pollutants** and exposure to **UV radiation** also accelerate skin aging.
- A blend of **four herbal extracts** (from rosemary, olive leaf, lemon verbena leaf, and Japanese pagoda tree leaf) defends the skin against the damaging effects of pollution and UV exposure.
- **Vitamin C** provides multiple benefits to skin health, such as promoting collagen formation and reducing dark-spot appearance.
- These ingredients support a healthy, hydrated, and more youthful-looking skin.

Lab studies show that this blend *completely* inhibits the pollution-induced increase in the expression of the **AhR receptor**, which can cause pigmented spots, inflammation, and oxidative stress.<sup>6,14</sup>

## Vitamin C Offers Added Support

**Vitamin C** offers additional benefits for skin health. In studies, **vitamin C** has been shown to:<sup>15-17</sup>

- Promote formation of **collagen**, the skin's main structural protein,
- Reduce **DNA** damage in the skin,
- Scavenge harmful **free radicals**, including oxidants from UV radiation,
- Improve skin **antioxidant** activity *in just two weeks*, and
- Inhibit **melanin** production, reducing the appearance of dark spots.

Most readers of this publication supplement with vitamin C based on compelling scientific findings of its ability to help maintain more youthful collagen levels.

## Summary

**Skin aging** is caused by a variety of factors.

The age-related *decrease* in production of skin **ceramides**, combined with the damaging effects of **pollutants** and **UV radiation**, leads to wrinkles, dryness, and age spots.

Taken orally, **rice-derived ceramides** have been clinically shown to enhance the skin's **barrier function** and boost overall skin hydration.

A blend of **four herbal extracts** protects against the destructive effects of pollution and UV exposure, improving the health and appearance of the skin.

**Vitamin C** offers a range of additional benefits to the skin, such as promoting collagen formation and reducing dark-spot appearance.

These ingredients, taken orally, can help hydrate, rejuvenate, and protect skin for a more youthful appearance. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

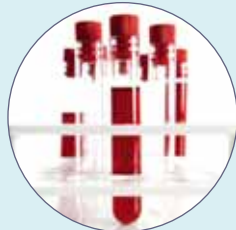
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#### References

1. *Open Orthop J.* 2012;6:143-9.
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**3-fold** improvement in skin moisturization and

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Just one capsule of **Daily Skin Defense** provides:

- **Rice-derived ceramides** designed to help improve **skin moisture**.<sup>2,3</sup>
- **Four Herbal Extracts** to support the skin's barrier function against environmental factors and reduce appearance of **wrinkle depth**.<sup>1</sup>
- **Vitamin C** to support **collagen** production and improve the skin's natural protection against the oxidative effects of UV light.<sup>4-6</sup>

# Youthful Skin Begins Inside



**Item #02423 • 30 vegetarian capsules**

1 bottle **\$24** • 4 bottles \$22 each

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#### References

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6. *Nutrients.* 2017 Aug 12;9(8):866.

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# SENOLYTICS

## A Major Anti-Aging Advance

BY MICHAEL DOWNEY







When old cells become dysfunctional, they're supposed to die off through a normal process called apoptosis.

But as we age, we accumulate too many of these malfunctioning (senescent) cells that refuse to die.

Sometimes referred to as "zombie cells," they pump out toxic compounds that degrade nearby cells and incite **chronic inflammation** that inflicts systemic damage.<sup>1</sup>

Compounds called **senolytics** *remove* senescent cells. Preclinical studies show that they can slow or **reverse** certain aspects of **aging**.<sup>2-5</sup>

Nutrients like **quercetin** and **theaflavins** (from black tea) have demonstrated **senolytic activities** and have been widely used in recent years.

The plant flavonoid **fisetin** is currently considered one of **the most powerful natural senolytics**.<sup>4,6-20</sup>

Its effects are dramatic. Elderly mice given **fisetin** had their **lifespans extended by nearly 10%**.<sup>4</sup> This may be analogous to a **75-year-old** human living about **7.5 years** longer.

The challenge up until now was that **fisetin** is converted into other compounds in the digestive tract. This means very little whole, unaltered fisetin is **absorbed** into the bloodstream.

Scientists have developed a method to increase **fisetin** blood levels up to **25 times** higher,<sup>21</sup> thus enabling **fisetin** to be distributed throughout the body.

Enlivened individuals today are taking this highly-absorbable **fisetin** by itself and/or combining it with a once-weekly high potency **quercetin + theaflavins** for enhanced **senolytic** effects.

## Senescent Cells and Aging

In youth, cells naturally eliminate themselves if they become damaged or dysfunctional. This process is called **apoptosis**.<sup>22</sup>

With age, however, we accumulate more **senescent cells** that emit toxic byproducts, that cause more cells to become senescent. These dysfunctional cells no longer perform basic functions. They instead inflict localized and systemic damage to our healthy cells.

**Senescent cells** undergo a series of transformations that result in their **secreting** high levels of **toxic compounds**, collectively referred to as **SASP** or **senescence-associated secretory phenotype**.

As a result, the buildup of **senescent cells** has been shown to **accelerate the aging process** and increase the risk of age-related diseases, including:<sup>23-30</sup>

- Diabetes,
- Obesity,
- Stroke,
- Vision loss,
- Neurodegenerative disorders,
- Osteoarthritis,
- Emphysema, and
- Cancer.

Research shows that just **one** senescent cell out of **7,000-15,000** healthy cells can initiate degenerative aging.<sup>31</sup>

*Removing **senescent** cells from the body can **reduce** the cellular drivers of aging and improve overall health.*<sup>32</sup>

That's where **senolytics** come in.

## Senolytics to the Rescue

**Senolytics** are compounds that enable the body to remove **senescent cells**.<sup>33,34</sup>

They work by **reactivating** the apoptosis switch in senescent cells. That causes these toxic cells to die and make room for healthy young cells.<sup>35</sup>

Published scientific studies demonstrate that **removing** senescent cells from the body improves markers of aging and prolongs lifespan in some models.<sup>28,32,33,35,36</sup>

In mice with **atherosclerosis**, removing senescent cells significantly inhibited the growth of arterial plaque and even caused it to regress.<sup>37</sup> This could be an important step in preventing heart and blood vessel disease.

In another study, a mouse model of **aging** showed that removing senescent cells benefited multiple tissues, while **delaying** the onset and slowing the progression of age-related disorders.<sup>28</sup>





## Fisetin: Today's Ultimate Senolytic

Scientists have studied many different nutrients, searching for effective **senolytics**.

**Fisetin** is the **most potent “on target” senolytic** known today.<sup>4</sup>

**Fisetin** is a flavonoid found in small amounts in strawberries, apples, persimmons, grapes, onions, and other plants. A cell study found that it eliminated about **70%** of senescent cells—while doing *no harm* to healthy human cells.<sup>5</sup>

These and other effects of fisetin have been shown to increase **longevity** in various animal models.<sup>2,15</sup>

Mice given fisetin lived an average of about 2.5 months longer, an almost **10% extension of lifespan**—even when treatment started at the **human** equivalent of **75 years** of age.<sup>4</sup>

## Other Benefits of Fisetin

The effects of **fisetin** go beyond its potent **senolytic** activity.

Fisetin also:

- Protects the **brain** in various models of neurodegenerative disorders,<sup>6-8,13-15,20</sup>
- Improves outcomes in people who have suffered **strokes**,<sup>18</sup>
- Helps prevent **malignant** changes inside cells,<sup>11,12,16,19</sup>
- In animal and experimental models, helps fight **obesity** and **type II diabetes** tendencies,<sup>9,10,17</sup>
- Reduces the risk of **atrial fibrillation** after a heart attack, in an animal study,<sup>38</sup>
- Reduces levels of **pro-inflammatory** mediators, in a study of colorectal patients,<sup>39</sup> and
- Based on results of preclinical studies, may inhibit cancer migration and growth and incite **cancer cell death**.<sup>16,40-45</sup>

Fisetin also has an ability to impact many of the same cellular pathways that **calorie restriction** does.<sup>2,15,46,47</sup> Reducing food intake through a **calorie-restricted diet** has been shown to slow aging, extend lifespan, and improve resistance to disease.<sup>48</sup>

## WHAT YOU NEED TO KNOW

### Removing Senescent Cells for Better Health

- With age, we accumulate **senescent cells**, dysfunctional cells that refuse to die off. These cells are associated with accelerated aging and age-related disease.
- **Senolytics** are compounds that can *remove* senescent cells, helping to maintain optimal function and youthful health. In preclinical studies, senolytics slow or even reverse aging.
- The compound **fisetin** is one of the most potent plant-derived senolytics ever discovered. In animal research, it effectively removes senescent cells and boosts longevity. Old mice given fisetin had their lifespans extended by nearly **10%**.
- **Quercetin** is another plant compound that has significant senolytic effects and improves markers of health. It is even more powerful when enhanced with senolytic black tea compounds called **theaflavins**.
- **Fisetin, quercetin, theaflavins, and apigenin** are nutrients with senolytic activity.

Until recently, there's been a challenge with oral fisetin: It is rapidly converted into other compounds in the gut. Scientists have solved this problem by *combining* fisetin with a fiber called **galactomannans**, isolated from the spice **fenugreek**.

This formulation has been shown to increase the **bioavailability** (absorption) of fisetin by as much as **25 times**, greatly enhancing its impact.<sup>21</sup>

## The Power of Quercetin

Before fisetin, quercetin, found in many fruits and vegetables, was one of the first plant-derived flavonoids to be tested as a senolytic.<sup>49</sup>

Quercetin has long been recognized for a range of benefits, including:

- Anti-inflammatory activity, shown to protect cells and tissues from injury,<sup>50-54</sup>
- Improved markers of aging and extended lifespan in lab studies,<sup>55-60</sup> and
- Reduction or prevention of age-related disease and dysfunction in human studies.<sup>61,62</sup>

The medical literature supporting the **senolytic** effects of quercetin has been growing over many years.<sup>32,33,35,60,63-65</sup>

In a study published in late 2019, quercetin successfully removed senescent cells in the kidneys of mice. This improved function and decreased the fibrosis (scarring) that leads to **kidney failure**.<sup>49</sup>

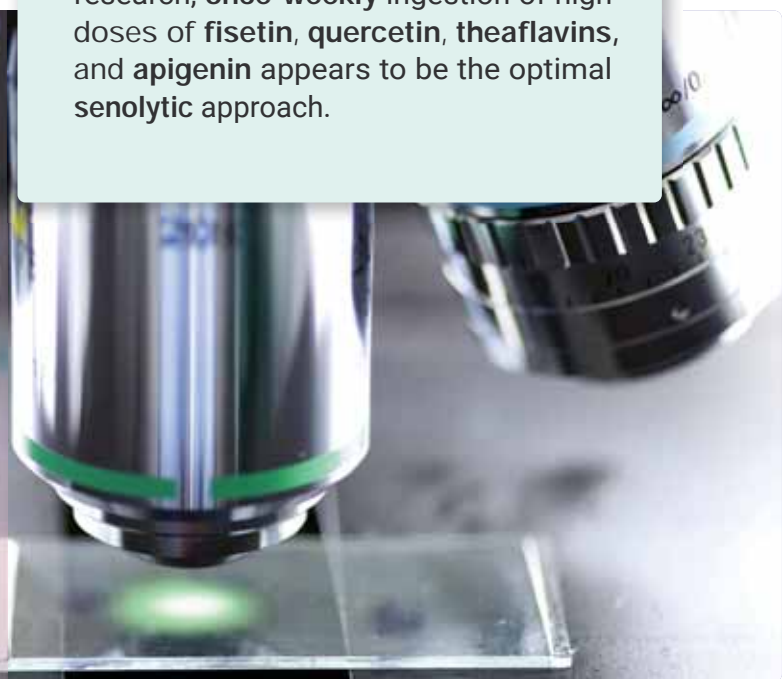
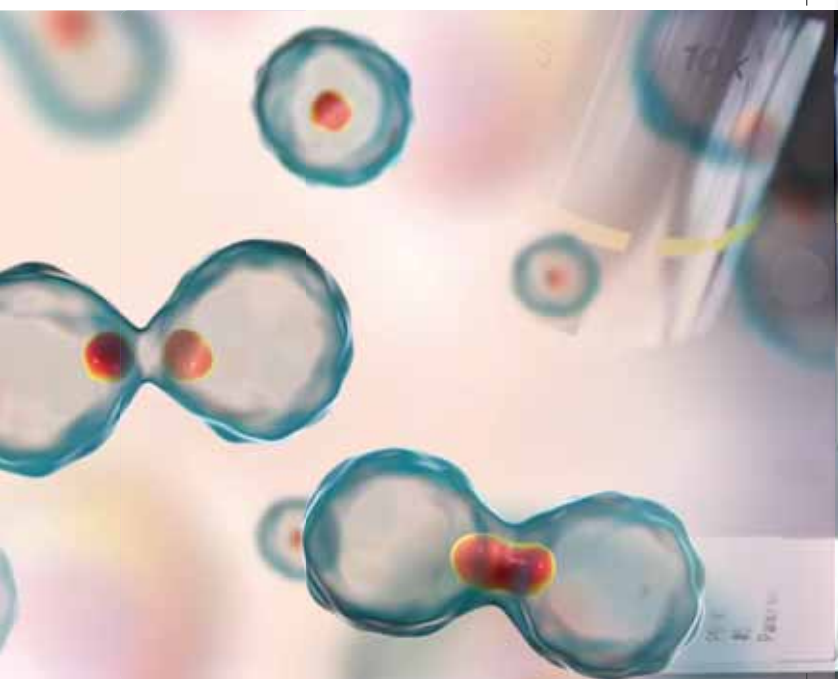
Quercetin can be difficult to absorb.<sup>66</sup> Scientists got around this problem by combining it with a type of fatty substance called a **phospholipid**. The phospholipid serves as a **carrier**, allowing much more quercetin to enter the bloodstream and exert its effects throughout the body.<sup>67</sup>

## Intermittent or Continual Therapy: Which Senolytic Program is Most Effective?

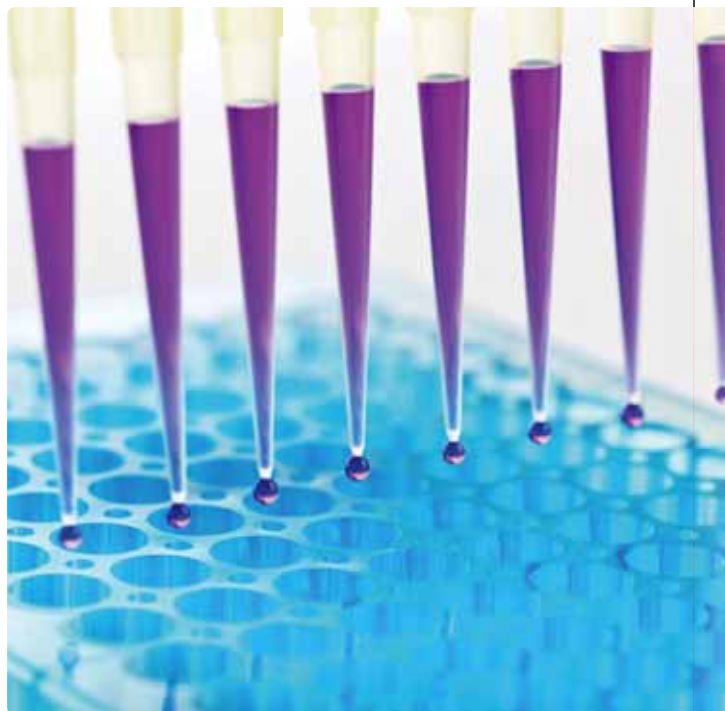
There's a great deal of debate in the longevity community about the ideal treatment regimen for **senolytic** therapies.

For now, **intermittent therapy** appears to be the best approach to reducing senescent cells.<sup>32,33,64</sup> Drugs that reduce expression of pro-inflammatory compounds secreted by senescent cells, for example, seem more effective when taken on an intermittent basis.<sup>76</sup>

Based upon the available preclinical research, **once-weekly** ingestion of high doses of **fisetin**, **quercetin**, **theaflavins**, and **apigenin** appears to be the optimal **senolytic** approach.







### Boosting Quercetin's Effects

Research has shown that quercetin works even *more effectively* when coupled with a chemotherapy drug, **dasatinib**.

When this combination was administered to old mice, its ability to eliminate senescent cells led to improvements in grip strength, coat condition, movement, and overall health.<sup>32</sup>

The first human study of this combination was published in 2019. Patients with **idiopathic pulmonary fibrosis** (a progressive lung disease) were given **100 mg/day** dasatinib and **1,250 mg/day** quercetin on three consecutive days per week for three weeks.<sup>68</sup>

This improved several measurements of **physical activity**, including distance walked and walking speed.

Scientists set out to identify a compound that would enhance quercetin's senolytic effects by the same mechanisms as dasatinib, but *without* the side effects of a cancer drug.<sup>69-72</sup>

The most effective candidate they found was a group of compounds in black tea called **theaflavins**.

In a similar way to dasatinib, **theaflavins** block an anti-apoptotic protein called **BCL-2**.<sup>69,73</sup> If you wonder what BCL stands for, it is "**B-cell lymphoma**."

A compound that blocks **BCL-2** might reduce risk of this common malignancy.

In a mouse study, **theaflavins** demonstrated significant **senolytic** effects.<sup>73</sup>

### Targeting Toxic Secretions Emitted by Senescent Cells

**Apigenin** is a flavonoid found in certain herbs, fruits, and vegetables.

In two recent studies, **apigenin** was found to *inhibit* the **SASP**, also known as the senescence-associated secretory phenotype. This resulted in a reduction of **pro-inflammatory** compounds produced by senescent cells.<sup>74,75</sup>

Reducing **inflammation** caused by the **SASP** while diminishing the **senescent cell burden** gives a two-pronged strategy for fighting this enemy of longevity.

**Quercetin** and **theaflavins** (from black tea) function via separate and complementary mechanisms to purge the body of **senescent cells**.

Fisetin, a strawberry flavonoid, has been shown to be the **most effective senolytic** when compared to a panel of flavonoids, removing aged, dysfunctional **senescent cells** in preclinical studies.

A multi-targeted approach utilizing highly absorbable **quercetin** and **fisetin**, plus **theaflavins**, and **apigenin**, can attack **cellular senescence** from multiple angles, helping to rid the body of the damage it causes.

## Summary

Old or dysfunctional cells promote **chronic inflammation** and contribute to loss of function and increased risk for age-related disease.

**Senolytics** can cleanse the body of these cells, improving organ function and preventing disease.

A plant extract called **fisetin** has been identified as the most powerful senolytic known so far. An innovative formulation has enhanced fisetin's absorption up to **25 times**.

**Fisetin** by itself or combined with other known senolytic ingredients such as **quercetin and theaflavins**, may provide *superior senolytic* benefits. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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The suggested dose of the new **Senolytic Activator®** is **3 capsules** once a week. Each bottle lasts 3 months and costs very little.



# BENFOTIAMINE

## Reduces Accelerated Aging

BY BEVERLY STAMOS







We know that too much **sugar** is bad for you. It causes diabetes, weight gain, and rots your teeth.

But the invisible harm that sugar causes goes beyond that.

A process known as **glycation** occurs when **glucose** in your bloodstream binds to **proteins, fats, and nucleic acids** in cells and tissues.

This causes the formation of **advanced glycation end-products** or **AGEs**.

Excessive glycation accelerates **aging** processes and contributes to many forms of **chronic disease**, from arterial blockage to dementia.<sup>1-4</sup>

A specialized form of **vitamin B1** called **benfotiamine** offers ***anti-glycation activity*** that may slow certain aging processes and maintain youthful tissue function.



## The Danger of Glycation

**Glucose** is the main sugar that circulates in the blood. Cells break it down and use it as an energy source.

But glucose has a dark side.

It can combine with other compounds like proteins and fats, and even nucleic acids.\* This process is known as **glycation**.

The result is **toxic** compounds being formed called **advanced glycation end-products (AGEs)**.<sup>3</sup>

AGEs damage cellular structures, particularly the body's **proteins**, and alter their function. The buildup of damaged proteins wreaks havoc on tissues throughout the body.

For example, **blood vessels** normally dilate or constrict to control blood flow. But with **damaged proteins** in their walls, blood vessels become stiff and unresponsive, hastening the onset of **cardiovascular disease**.<sup>3</sup>

AGEs also bind to cell receptors that activate **chronic inflammation**.<sup>3</sup> This inflammation is a major cause of accelerated aging and age-related disease.<sup>5</sup>

The *higher* glucose levels are, the *more* glycation occurs.

This is an important reason why **diabetes** is so dangerous. When glucose levels are chronically high, more toxic **glycation end-products** are created.

\* Nucleic acids are present in living cells, especially cellular DNA and RNA.

But glycation occurs in *all* aging adults, not just diabetics, affecting every tissue in the body.

Glycation contributes to:

- Dementia,
- Heart and blood vessel disease,
- Kidney failure,
- Macular degeneration and vision loss,
- Nerve dysfunction,
- Osteoarthritis,
- Cancer,
- Aging, wrinkled skin,
- And more.<sup>2-4,6-14</sup>

In elderly subjects, higher levels of AGEs detected on blood tests are associated with poor physical function.<sup>15,16</sup>

Glycation slowly destroys the body from the inside out.





## High Glucose Harms the Brain

The **brain** is constantly taking up glucose from the blood to use for energy.

The link between glucose metabolism and brain disease is so strong that many doctors and researchers have taken to calling **Alzheimer's disease** "**type III diabetes**."<sup>17,18</sup>

There are a variety of ways that excess glucose harms brain function.<sup>19-22</sup>

In the short term, **hyperglycemia** (high blood glucose) has a significant impact on mood and cognitive performance.

In patients with **type II diabetes**, one study found that information processing, memory, and attention were all impaired when blood **glucose** levels were **high**.<sup>23</sup>

These individuals also tended to have a more depressed and anxious mood and reduced energy and arousal.<sup>23</sup>

In the **long term**, glycation contributes to chronic loss of brain function and, eventually, **dementia**.<sup>19-22</sup>

Research shows that people with diabetes have, on average, **double** the risk of developing dementia than non-diabetic individuals.<sup>24</sup>

Among diabetics, those with *poor* blood glucose control have a **40%** greater risk of dementia than those with better glucose control.<sup>25</sup> Even patients with **pre-diabetes** were found to be **18%** more likely to develop dementia than people with normal glucose levels.

## How Benfotiamine Helps

There *are* ways to prevent glycation damage.

Cutting back on sugar can help. But even if you cut out *all* simple sugars in the diet, the **liver** will produce a minimum level of blood glucose to ensure your survival via a process known as gluconeogenesis.

**Glycation** still occurs, though at a slower rate.

But there is more you can do.

**Thiamine**, or **vitamin B1**, is a nutrient required for various processes in the body. However, thiamine is not easily absorbed into the body. Researchers have found that a special form of thiamine can help **prevent glycation**.<sup>26,27</sup>

**Benfotiamine** is a fat-soluble form of thiamine that is significantly more **bioavailable** (absorbable).<sup>26,27</sup>

Taken orally, benfotiamine is rapidly absorbed and reaches much higher levels in the blood and in cells. Research shows that a single dose of benfotiamine leads to a **five-times** greater level in the blood than an equivalent dose of thiamine.<sup>26,27</sup>



## WHAT YOU NEED TO KNOW

### Fighting Damage Done by Glycation

- Blood sugar, or **glucose**, is an important fuel for cells. But it can combine with other compounds in a process known as **glycation**. This damages cellular structures and compromises their function.
- Glycation and the buildup of **advanced glycation end-products** in bodily tissues is a major contributor to aging and age-related chronic disease.
- Scientists have identified a form of vitamin B1, **benfotiamine**, which is highly bioavailable and able to protect against glycation in multiple ways.
- In clinical studies, oral benfotiamine intake has already shown clear benefits for **diabetic neurological complications**, **mild cognitive impairment**, and **Alzheimer's disease**.
- Preliminary research shows that it has promise in slowing aging and lowering risk for other forms of chronic disease.
- **Life Extension**<sup>®</sup> suggests taking **250-1,000 mg** of benfotiamine daily to protect the body's tissues against glycation.



## Glycation in Food

Glycation doesn't just happen in your body. It can also take place *in your food*.

That means when you eat, you may take in significant amounts of toxic **advanced glycation end-products (AGEs)**.

Foods that contain high levels of glycated compounds include red meats, sugary and processed foods, and those cooked with **high heat**. Deep-fried, pan-fried, and roasted foods are among the worst culprits.

Studies estimate that about **10%-30%** of ingested AGEs are absorbed into the body, where they can do serious damage.<sup>14</sup>

In one study, subjects with type II diabetes were given a meal with a **high AGE content**.<sup>38</sup> Within hours, *blood levels* of AGEs increased.

This caused immediate damage to tissues. Researchers observed a jump in serum markers of **endothelial dysfunction** and **oxidative stress**. This worsens blood vessel disease and increases the risk for future heart attack and stroke.

**Benfotiamine** can *prevent* dietary sources of AGEs from doing damage. In the study, some of the patients given the meal high in AGEs were *also* given benfotiamine.<sup>38</sup> In those people, the peak blood AGE level was significantly reduced and the negative changes in blood vessel function were *completely prevented*.

Benfotiamine blocks several tissue-damaging mechanisms, one of them being the **advanced glycation end-products (AGEs)** formation pathway.<sup>26,27</sup> It is also able to limit effects of AGEs by reducing inflammation and harmful AGE-triggered changes.<sup>27</sup>

Through these actions, benfotiamine provides powerful protection against the aging process and development of disease.

## Combating Sugar-Related Disease

**Benfotiamine** has been explored for the treatment or prevention of age- and diabetes-related disorders.

Given the excessive glycation that occurs with high blood glucose levels in diabetic patients, and benfotiamine's ability to combat this damage, it is no surprise that it has been studied as a treatment for complications of **diabetes**.<sup>28-31</sup>

For example, benfotiamine has been shown to help treat and manage **neuropathy**, a painful nerve disease common in diabetics.<sup>29,30,32-34</sup>

It has also shown benefits for management of cognitive decline in non-diabetic subjects, ranging from mild cognitive impairment to moderate Alzheimer's disease.

In one randomized controlled trial published in 2020, scientists from Columbia University and Weill Cornell Medicine treated patients with cognitive deficits ranging from mild cognitive impairment to mild Alzheimer's dementia with either **300 mg** of benfotiamine twice daily for one year, or placebo.<sup>35</sup>



Over the year, *decline* in cognitive function (measured by the **Clinical Dementia Rating Scale**) was **77% less** in the group receiving **benfotiamine**. This means that it slowed the clinical progression of the condition.

Benfotiamine also prevented AGEs from increasing. This means it interrupted toxic glycation reactions, suggesting it slowed an important contributor to biochemical aging.<sup>35</sup>

In an earlier pilot trial in five patients with mild to moderate Alzheimer's, **300 mg** of benfotiamine daily for 18 months led to a **cognitive improvement**, not just a slowing of deterioration. The average *increase* on the **Mini-Mental State Exam**, the most common tool for assessing the severity of dementia, averaged **3.2 points**.<sup>36</sup>

Considering that a change as low as **1 point** on this exam is considered "meaningful," this **3.2 point** improvement is remarkable.<sup>37</sup>

Benfotiamine's ability to prevent glycation, along with its anti-inflammatory and antioxidant properties, has great promise in slowing the aging process and reducing risk for many other diseases as well.<sup>27</sup>

**Life Extension®** suggests taking **250-1,000 mg** of benfotiamine daily to protect the body's tissues against glycation. Those with worsening glycemic control should consider the higher dose range.

## Summary

Blood **glucose**, both in diabetics and non-diabetics, can combine with other compounds in a process known as **glycation**.

This results in toxic end-products that cause significant damage to cells and tissues.

Glycation has been shown to be a major driver of **aging, chronic disease**, and complications of diabetes.

Scientists have found that a highly bioavailable form of vitamin B1 called **benfotiamine** effectively reduces buildup of glycated compounds in the body.

Benfotiamine intake has shown benefits in treating **diabetic neuropathy, mild cognitive impairment**, and **Alzheimer's disease** in human trials.

Research also suggests that benfotiamine may be beneficial in slowing the aging process and lowering risk for many other age-related chronic diseases. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.



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# CoQ10: More Than Just Heart Health

BY CHANCELLOR FALOON

While CoQ10 is best known for promoting heart health, research is continually showing a diverse range of body-wide applications.

- **CoQ10 Improves Metabolic Syndrome**

A meta-analysis was done of trials that tested coenzyme Q10 (CoQ10) on patients with metabolic syndrome. Compared to a placebo, CoQ10 supplementation *lowered* inflammation markers and *increased* levels of a cell-signaling protein related to improved regulation of glucose and fatty-acid breakdown.<sup>1</sup>

- **CoQ10 Increases Blood Flow**

In a clinical trial, CoQ10 (ubiquinol) **improved cardiovascular function**, as shown by *increased* flow-mediated dilation<sup>2</sup> (widening of an artery when blood flow increases) and levels of nitric oxide (which aids in dilation). Harmful **LDL oxidation** was reduced with a higher dose.<sup>3</sup>

- **CoQ10 Enhances Exercise Performance**

Exercise performance and several biomarkers related to fatigue were improved in mice and humans given CoQ10 (ubiquinol). Liver and muscle glycogen content increased, providing the body with more fuel for prolonged exercise.<sup>4-6</sup>

- **CoQ10 Increases Cellular Energy**

In a cell study, CoQ10 (ubiquinol) was able to *prevent* age-induced **oxidative stress**, increase the formation of **new mitochondria** (the cells' energy generators), and was associated with the removal of old, damaged mitochondria.<sup>7</sup>

- **CoQ10 Protects Aging Heart Muscle**

A recent review shows supporting evidence that CoQ10 can benefit heart failure patients by preventing age-related reductions in myocardial (heart muscle) ATP, the powerhouse of our cells.<sup>8</sup>

- **CoQ10 Mediates Inflammation**

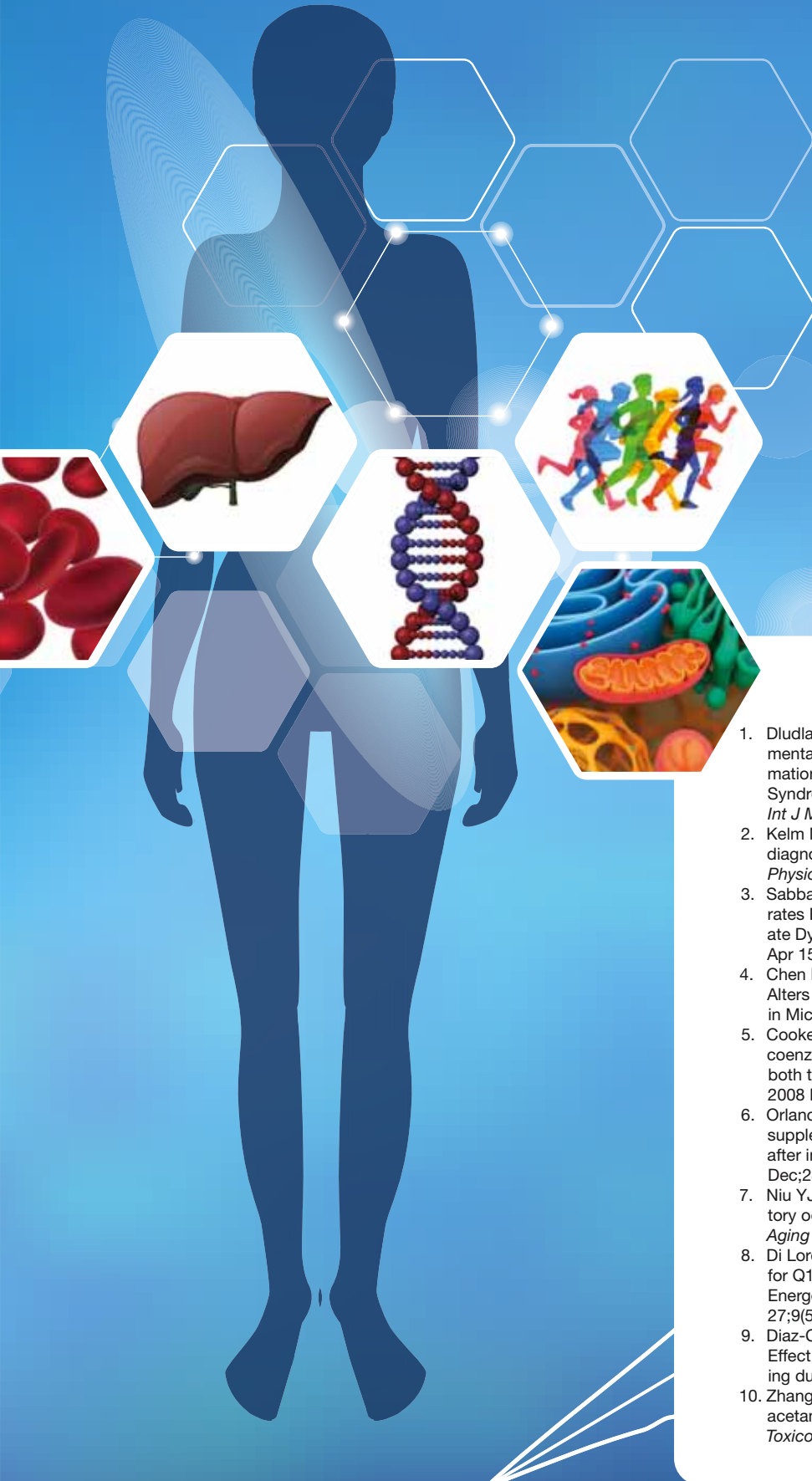
To see if CoQ10 could prevent damage that may occur with **strenuous exercise**, 100 firemen were randomized to receive CoQ10 (ubiquinol) or a placebo. The CoQ10 group had significantly improved **hematological** (blood) parameters, *increases* in beneficial growth factors and anti-inflammatory cytokines, and a *decrease* in pro-inflammatory cytokines.<sup>9</sup>

- **CoQ10 Protects Against Acetaminophen Liver Injury**

A study in mice found that CoQ10 protected against acetaminophen- (Tylenol®) induced liver injury. CoQ10 also enhanced removal of damaged mitochondria.<sup>10</sup>

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.





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# Powerful Defense Against Bloating and Indigestion

BY CHANCELLOR FALOON





After-meal **bloating** is one of the most common and difficult digestive issues.

Up to **30%** of people experience bloating. It tends to come hand-in-hand with other gastrointestinal disorders, such as **dyspepsia** (indigestion), irritable bowel syndrome, and constipation.<sup>1</sup>

Research has identified **four plant compounds** that help relieve bloating and other gastrointestinal problems.

In a clinical trial, **63.1%** of subjects taking an **artichoke-ginger** blend had significantly reduced feelings of bloating, gassiness, nausea, and other symptoms of indigestion.<sup>2</sup>

In another trial, a **fennel-curcumin** combination relieved symptoms of **irritable bowel syndrome**, including bloating and stomach pain, by more than **50%**. This fennel-curcumin blend prevented *all* symptoms in **25.9%** of users.<sup>3</sup>

Taken together, these **four plant compounds** can provide partial or complete relief from digestive miseries.

## What Causes Bloating?

**Bloating** is characterized by trapped gas, abdominal pressure and pain, and a feeling of excessive fullness. It is one of the most frequently reported gastrointestinal issues.<sup>1</sup>

The causes are complex. There can be a wide range of contributing factors, notably including food intolerance, small intestinal bacterial overgrowth, and inflammatory conditions.<sup>1</sup>

But research has revealed that four plant compounds can safely relieve bloating and improve the overall health of your digestive system.

## Fennel-Curcumin Relieves Pain and Gas

**Fennel** and **curcumin** have traditionally been used to aid digestion.

Seeds from fennel, a plant known for its licorice flavor, have long been consumed after meals to promote **digestion** and prevent **flatulence**.<sup>4</sup>

In vitro research shows that fennel reduces gas production by inhibiting the activity of a methane-producing bacterial enzyme.<sup>5</sup>

In addition, clinical trials have shown that fennel seeds, tea, and seed oil stimulate gastrointestinal function, improving gastric motility.<sup>3,6,7</sup>

Fennel also has an antispasmodic effect, reducing irregular muscle contractions that impair normal gut motility.<sup>3</sup>

Researchers combined **fennel seed oil** and a **low-dose curcumin** in a clinical trial to test their effect on bloating and abdominal pain.<sup>3</sup>

## Easing Irritable Bowel Syndrome

For the trial, researchers enlisted 121 patients between the age of 18-60 who suffered from **irritable bowel syndrome**. They gave them either a blend of **42 mg of curcumin** and **25 mg of fennel seed oil** or a placebo, twice daily.<sup>3</sup>

After 30 days, those taking the **fennel-curcumin** blend reported an average **50%** decrease in bloating, abdominal pain, and other irritable bowel syndrome symptoms. This was nearly *double* the **26.1%** decrease in the placebo group.

All symptoms were improved by treatment. Among those taking fennel-curcumin, **25.9%** became **completely symptom-free**, compared to just **6.8%** of placebo recipients.

The treated group also reported a significant improvement in irritable bowel syndrome-related quality of life, with no adverse effects.

## Artichoke-Ginger Mix Aids Digestion

**Artichoke** influences the production of **bile** from the liver, which helps break down fats, absorb fat-soluble vitamins, and speed up digestion.<sup>8</sup> Italians traditionally serve an artichoke and herbal liqueur after dinner to assist with digestion.

**Ginger** has been shown in human studies to promote **gastric motility**, the movement of food out of the stomach and into the small intestine.<sup>9,10</sup>

A combination of **20 mg of ginger root extract** and **100 mg of artichoke leaf extract** led to substantial gastrointestinal improvement in a clinical trial.<sup>2</sup>







## WHAT YOU NEED TO KNOW

### Relief for Post-Meal Problems

- Bloating is one of the most common gastrointestinal symptoms, marked by a feeling of excessive fullness, gas, and abdominal pressure and pain.
- Scientists have identified four clinically effective compounds that target the *underlying causes* of bloating.
- A blend of artichoke leaf and ginger root extracts relieves symptoms of dyspepsia (indigestion), including bloating, nausea, vomiting, and upper abdominal pain.
- A mix of fennel seed oil and curcumin decreases bloating, abdominal pain, and other severe symptoms of irritable bowel syndrome.
- Taken together, ginger root, artichoke leaf, fennel seed oil, and curcumin may help prevent or significantly reduce gastrointestinal distress and improve quality of life.

The study recruited 126 patients with **functional dyspepsia** (recurring and unexplained indigestion) to receive the combination or a placebo.

Patients rated the severity of six dyspepsia symptoms: fullness, bloating, feeling full after only a small amount of food, nausea, vomiting, and **epigastric** (upper abdominal) pain.

In just two weeks, **44.6%** of participants taking the artichoke-ginger blend had significant improvement in digestive symptoms, compared to **13.1%** of placebo users.

After four weeks, **63.1%** of those in the treatment group reported marked reductions in digestive symptoms, compared to only **24.6%** in the placebo group.

### Summary

After-meal **bloating**, and other gastrointestinal disturbances can impair our quality of life.

Researchers have identified four plant compounds that target multiple causes of bloating and have shown clinical effectiveness.

In one clinical trial, **63.1%** of subjects taking an **artichoke-ginger** blend experienced significantly reduced gastrointestinal disturbances.

In another trial, a combination of **fennel** and **curcumin** was able to completely prevent all gastrointestinal symptoms in **25.9%** of users.

Together, compounds from these four plants may promote a **healthier digestive system** and help protect against bloating, gas, nausea, and other gastrointestinal issues. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

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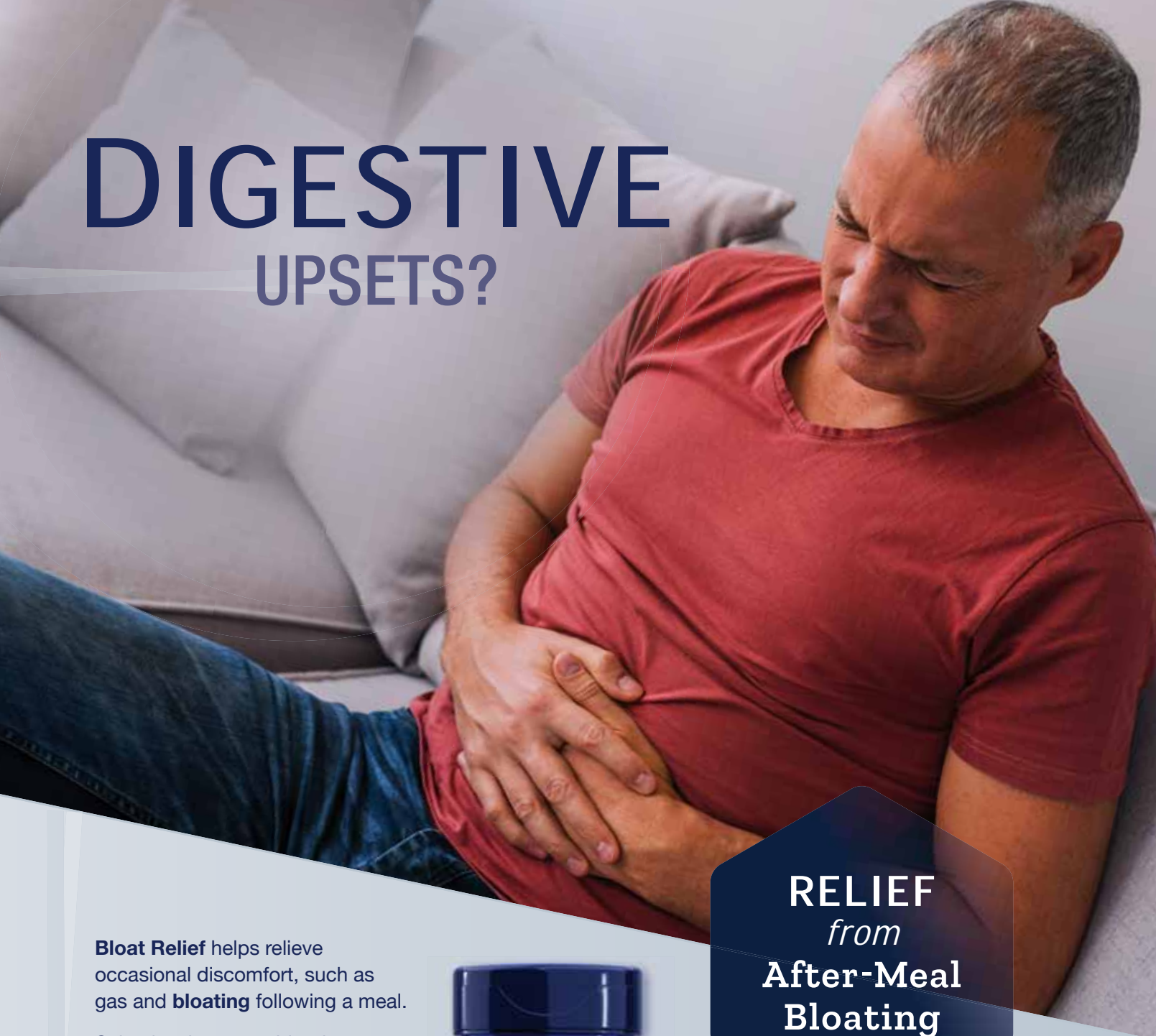
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\* *Br J Pharmacol.* 2004 Mar;141(5):825-30.

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# Brighten and Illuminate Dull, Uneven Skin Tone

BY ROBERT GOLDFADEN AND GARY GOLDFADEN, MD



Age spots and dark patches create dull, uneven skin tone that robs youthful appearance.

These undesirable changes result from increased amounts of the skin's main pigment, **melanin**, as we age.<sup>1-3</sup>

Scientists have found that two topically-applied compounds, **glutathione** and **niacinamide**, inhibit multiple stages of melanin *synthesis* to produce a skin-brightening effect.

Additional topical compounds promote the appearance of brighter skin by boosting **collagen synthesis** and enhancing **DNA repair**.



## Targeting Multiple Stages of Melanin Production

When sunlight hits the skin, specialized cells called melanocytes produce small amounts of the pigment **melanin** to help protect against the damaging effects of ultraviolet rays.<sup>4,5</sup>

Chronic sun exposure, however, along with other factors such as heredity and hormonal changes, trigger melanocytes to excessively produce **melanin**.<sup>6-8</sup>

This manifests as **age spots** and difficult-to-treat melasma (dark, discolored patches on skin).

As the years pass, the process of **melanin synthesis** becomes dysregulated and contributes to older-looking skin.

Two compounds have been shown to impede **melanin** production to favorably modulate skin pigmentation.

## Glutathione Inhibits Tyrosinase Activation

**Glutathione** is a naturally occurring tripeptide found inside every cell, where it plays a crucial role in antioxidant defense, immunity, and detoxification.<sup>12,13</sup>

In addition, glutathione has been shown to exhibit **anti-melanogenic** properties.<sup>14</sup>

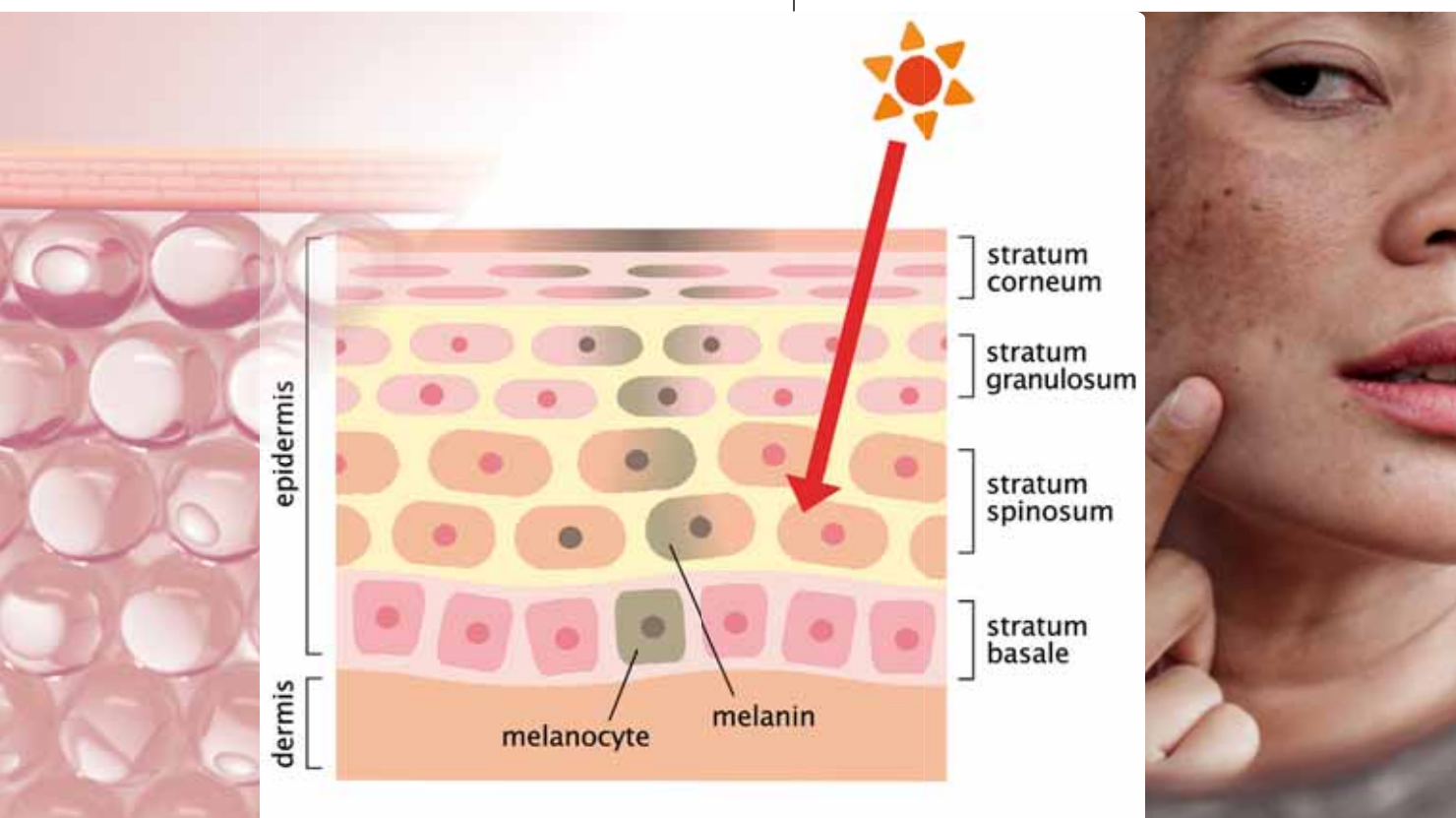
It binds to the copper-containing site of tyrosinase, in turn preventing its activation, and thus the signal to turn on **melanin output**.<sup>14,15</sup> Thanks to its potent antioxidant effects, glutathione combats UV-induced free radicals that induce tyrosinase activity.<sup>5,16</sup>

Human studies show that topical glutathione results in a clearer and more even complexion. In a randomized, double-blind, controlled study, female subjects topically applied glutathione twice daily to one side of the face and a placebo to the other for 10 weeks.<sup>17</sup>

Compared to the placebo group, the glutathione-treated group showed a significant decrease in **melanin index**—an indicator of the skin's melanin content—as well as **diminished wrinkles** and **improved skin** moisture and smoothness.<sup>17</sup>

Other research has established the effectiveness of **topical glutathione** to treat a common pigmentation disorder known as melasma that affects mostly women in the facial area.<sup>18,19</sup>

In one clinical study, topical glutathione significantly reduced the **melasma** area and severity index compared to a placebo, which translated into brighter skin for participants at the study's end.<sup>19</sup> This is noteworthy, since melasma has been historically difficult to treat.<sup>20</sup>







### Niacinamide and Skin Pigmentation

**Niacinamide** is a form of niacin (vitamin B3) shown to combat skin aging by boosting antioxidant capacity, improving epidermal barrier function, and modulating pigmentation.<sup>21</sup>

Randomized, double-blind, placebo-controlled human trials demonstrate that topical **niacinamide** significantly decreases facial skin yellowing, blotchiness, wrinkling, and excess pigmentation after three months.<sup>22,23</sup>

In a double-blind clinical trial, females aged 25-60 with multiple types of brown patches, topically applied **niacinamide** twice daily to one side of the face and a placebo to the other for eight weeks.<sup>24</sup>

Compared to baseline, the treatment group decreased total area of hyperpigmentation by **25%** versus only **15%** in the placebo group. Topical niacinamide was well-tolerated by participants.<sup>24</sup>

Researchers found that topical niacinamide was comparable to the gold-standard hydroquinone for treating melasma, but importantly accomplished this with fewer side effects.<sup>25</sup>

Clinical improvements in the niacinamide-treated group were correlated with skin biopsy evidence of significant reductions in epidermal melanin and inflammation.<sup>25</sup>

### WHAT YOU NEED TO KNOW

## Eliminate Age-Related Skin Discoloration

- Melanin is the predominant pigment in the skin that protects against damaging ultraviolet rays.
- Chronic sun exposure, along with other factors like heredity and hormonal changes, cause melanocytes to overproduce melanin.
- This manifests in the outward appearance of dull skin, uneven skin tone, age spots, dark patches, and melasma.
- Researchers have found two compounds that work together to inhibit multiple stages of melanin synthesis.
- Glutathione is a tripeptide that slows down tyrosinase activity by binding to its copper-containing active site and combating UV-induced oxidative stress.
- Niacinamide is a form of vitamin B3 that blocks the transfer of melanin-filled melanosomes from melanocytes to keratinocytes on the skin's surface.
- Additional agents—palmitoyl tripeptide-5, acetyl hexapeptide-51 amide, *Aspalathus linearis* leaf extract—promote the appearance of brighter skin by boosting collagen synthesis, enhancing DNA repair, and exerting potent antioxidant effects.

## Additional Compounds Support Brighter Skin

While **glutathione** and **niacinamide** work to normalize **melanin** output, several other compounds have been shown to support the appearance of more luminous skin by protecting and **rebuilding** the skin's underlying architecture. They are:

### 1. Palmitoyl Tripeptide-5

The loss of collagen as we age results in dry, dull-looking skin accompanied by wrinkles and increased pigmentation.

Scientists have discovered that **palmitoyl tripeptide-5** stimulates **collagen synthesis**.<sup>26</sup>

Together with other peptides, palmitoyl tripeptide-5 has been shown in clinical trials to reduce fine lines and wrinkles, as well as improve skin texture, tone, and radiance.<sup>26,27</sup> In other words, palmitoyl tripeptide-5 makes aging skin appear more plump, youthful, and radiant.

### 2. Acetyl Hexapeptide-51 Amide

Environmental factors and internal aging inflict **DNA damage** that, if left unrepaired, can add years to your perceived age. **Acetyl hexapeptide-51 amide** has been found to protect against DNA damage and switch on beneficial genes involved in DNA repair.<sup>28</sup>

In the laboratory, **acetyl hexapeptide-51** amide produced a **2.7-fold increase** in **DNA repair** pathways when exposed to human skin cells, compared to a control.<sup>28</sup>

This explains the finding of a later study in which humans topically applying acetyl hexapeptide-51 amide after exposure to ultraviolet light had **13.7% less DNA damage** than controls.<sup>28</sup> By preserving DNA integrity, acetyl hexapeptide-51 amide ensures the continuous production of new skin cells that have a fresh, more radiant appearance.





### 3. *Aspalathus linearis* Leaf Extract

Overexposure to ultraviolet radiation generates a storm of free radicals and oxidative stress that paves the way for wrinkles, fine lines, mottled pigmentation, and skin cancer.

***Aspalathus linearis*** is a South African plant well-known for its potent antioxidant and anti-inflammatory properties that scavenge free radicals, and provides significant protection against sun-induced skin damage.<sup>29,30</sup>

### Summary

The excessive output of the skin's **melanin** produces an uneven pigmentation that can make your skin appear older.

Topical **glutathione** and **niacinamide** have been shown to normalize melanin output to fade age spots, dark patches, and melasma.

Several other agents—palmitoyl tripeptide-5, acetyl hexapeptide-51 amide, *Aspalathus linearis* leaf extract—have been shown to aid in the appearance of brighter skin. •

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

Gary Goldfaden, MD, is a clinical dermatologist and lifetime member of the American Academy of Dermatology. He is the founder of Academy Dermatology in Hollywood, FL, and Cosmesis Skin Care. Dr. Goldfaden is a member of the **Life Extension®** Medical Advisory Board. All Cosmesis products are available online.

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# Heart Attacks Are Not Worth Dying For

BY MICHAEL OZNER, M.D.



**Michael Ozner** is a board-certified cardiologist and Medical Director of Wellness and Prevention at Baptist Health South Florida. He has dedicated his career to the eradication of atherosclerotic cardiovascular disease, namely heart attacks and strokes.

In his new book, *Heart Attacks Are Not Worth Dying For*, Dr. Ozner shares his revolutionary approach to ending heart disease, an epidemic that kills nearly 18 million people every year worldwide.

Dr. Ozner discusses a paradigm shift about how we can stabilize, regress and, in some cases, eradicate the buildup of fatty deposits in the artery walls, called atherosclerotic plaques. This can significantly lower the risk of heart attacks and other vascular catastrophes.

His latest book provides a straightforward pathway written for patients and their doctors to end the devastation of heart disease and live a longer life.

As a primary course of action, Dr. Ozner advocates making lifestyle changes that include the Mediterranean diet, exercise, stress reduction, smoking cessation, and quality sleep.

But many people are not able to achieve optimal heart health just through these measures.

For those individuals, Dr. Ozner explains how utilizing lifestyle interventions, advanced blood testing, vascular imaging, and highly effective medications (when needed) can safely reduce and potentially eliminate risk of vascular disease and coronary heart disease.

In this exclusive interview, Dr. Ozner talks about the root cause of heart disease—and the steps you can take to eliminate cardiovascular disease risk factors and achieve heart health and longevity.

—LAURIE MATHENA

**LE:** What does the latest research reveal about heart disease?

**Dr. Ozner:** As a preventive cardiologist, I have been in the trenches, fighting this disease for decades. We have recently made tremendous progress in our ability to identify and remove the root cause of this disease and the risk factors that fan the flames in the fire of this epidemic.

The amazing thing is that heart disease isn't the inevitable consequence of aging. We know what to do to prevent it. And we now know what to do to reverse it!

**LE:** How can coronary heart disease be prevented?

**Dr. Ozner:** We can prevent coronary heart disease by attacking and eliminating the primary cause—an excess number of cholesterol—and triglyceride-carrying particles called lipoproteins.

When there are too many potentially harmful (apoB) lipoprotein particles in the bloodstream, they can enter the blood vessel wall and lead to an atherosclerotic plaque. A heart attack is the result of a plaque rupture.

**LE:** How is our modern Western diet contributing to the heart disease epidemic?

**Dr. Ozner:** Unfortunately, many of the foods that make up our traditional Western diet are toxic to our bodies. Consuming unhealthy food is like putting diesel fuel in a gasoline-powered car—it simply does not work. We are not genetically programmed to function on processed food!

In fact, processed food is directly related to the ever-increasing spikes in obesity, hypertension, diabetes, heart disease, stroke, and yes, death. The toxic American diet is loaded with preservatives, sodium, refined sugar, and bad fats.

**LE:** What's the alternative?

**Dr. Ozner:** Research studies have shown that those following a traditional Mediterranean diet and lifestyle suffer significantly less heart disease and are far less likely to die from a heart attack.

Researchers from Italy recently looked at all studies through June 2010 that assessed the benefits

of the Mediterranean diet, and published them in the *American Journal of Clinical Nutrition*.<sup>1</sup> They found that the Mediterranean diet was associated with a statistically significant reduction of overall mortality, as well as cardiovascular mortality, cancer mortality, and neurodegenerative diseases.

But even more compelling is research showing that those who switch to a Mediterranean diet and lifestyle share in the same health benefits (including fewer heart attacks, a longer life expectancy, and a reduced risk of cancer), regardless of where they live or what their diets were like before.

**LE:** What about exercise?

**Dr. Ozner:** Dozens of clinical studies support the beneficial impact that exercise has on health. Regarding hypertension, the scientific literature shows that, on average, exercise decreases blood pressure in about **75%** of all people with hypertension.<sup>2</sup>

Clinical studies have demonstrated that those who engage in regular physical activity significantly reduce their risk of a heart attack.<sup>3</sup>

Exercise also has been shown to lower total cholesterol, raise “good” HDL cholesterol, lower triglycerides, and make the “bad” LDL cholesterol particles larger.

Larger LDL particles are less likely than smaller particles to get trapped in the arterial wall, become oxidized, and form a plaque that can eventually rupture and lead to a heart attack.

**LE:** What if lifestyle changes alone aren't enough to lower cholesterol and triglyceride levels?







**Dr. Ozner:** It is often said that people would be able to prevent this devastating disease if they would only follow a healthy lifestyle. Sadly, the reality is that most people are not compliant with healthy lifestyle choices, and sometimes lifestyle changes are not enough to stop the devastation of heart disease.

The good news is that there has been a “revolution” in heart disease prevention over the past decade. This has resulted in major breakthroughs in our battle against heart attack risk factors.

Over the past decade, we have made tremendous strides in developing highly effective medications that can stabilize, reduce, and in some cases eliminate blockages in our arteries. These therapeutic advances have led to a marked reduction in heart attacks and strokes.

New medications have been developed that significantly enhance the lowering of LDL cholesterol, triglycerides, lipoprotein (a), and vascular inflammation.

**LE:** Does this include statin drugs?

**Dr. Ozner:** Yes. Statins have become the first-line medication to lower cholesterol. Most importantly, numerous statin trials have demonstrated a significant reduction in heart attack risk in patients with elevated LDL cholesterol.

Popular brands include Crestor® (rosuvastatin), Lipitor® (atorvastatin) and Zocor® (simvastatin). Since they are available as generics, they are very cost effective.

**LE:** Statin medications have been available for decades, but they have not solved the heart attack pandemic. Why is this?

**Dr. Ozner:** The reason for this is that statins are limited in how much they can lower LDL cholesterol. Studies have shown that statins lower heart attack risk by about **35%**—well, what about the **65%** who have heart attacks despite taking statin medications?

This problem has been solved with the advent of new medications. These new medications allow us to achieve low LDL cholesterol levels that heretofore we have been unable to achieve with lifestyle intervention and statins. We now have the necessary “arrows in the quiver” to significantly lower the risk of heart attacks, strokes and vascular disease. We are now in a position to defeat this formidable enemy called cardiovascular disease.

Cholesterol-absorption inhibitors (ezetimibe or Zetia) can lower LDL cholesterol an additional **15%** to

**25%** when added to statins.<sup>4</sup> Clinical trials have shown that these medications are safe and lower heart attack risk compared to statin therapy alone.

The most promising new medications are known as PCSK9 inhibitors. When added to statins, there can be a further **50% to 60%** reduction in LDL cholesterol,<sup>5</sup> resulting in LDL levels that we have not been able to achieve before—levels as low as **20 mg/dL** and less! When it comes to LDL cholesterol, it has been shown that “lower is better”—the lower the LDL cholesterol, the lower is the risk of heart attack. It has also been shown in clinical studies that “earlier is better”—the earlier in life we can achieve normal LDL cholesterol, the lower the subsequent risk of cardiac events.

**LE:** Is it safe to reduce LDL this low?

**Dr. Ozner:** Clinical trials have demonstrated that there are no significant adverse effects of lowering LDL cholesterol with statins, cholesterol-absorption inhibitors, PCSK9 inhibitors or PCSK9 interfering agents. Studies have also shown that individuals genetically predisposed to low LDL cholesterol levels over a lifetime had no adverse effects and had a very low incidence of cardiovascular disease.

**LE:** Can you tell us more about PCSK9 inhibitors?

**Dr. Ozner:** PCSK9 inhibitors are one of the more recent and exciting medications that have been developed to lower LDL cholesterol.

PCSK9 is a protein that decreases the amount of LDL cholesterol that can be removed from the bloodstream by the liver. By inhibiting PCSK9, we can now significantly lower LDL cholesterol.

Clinical trials have demonstrated a significant lowering of LDL cholesterol levels by **50%** or greater on top of statins.<sup>5</sup>

Most importantly, PCSK9 clinical-outcome trials (Fourier and Odyssey Outcomes) have shown that PCSK9 inhibitors are safe and lead to a significant reduction in cardiovascular events.

Repatha® (evolocumab) and Praluent® (alirocumab) are PCSK9 inhibitors approved for use in the United States, and they are given by subcutaneous injection every two to four weeks.

The most exciting new medication is inclisiran, an interfering agent that reduces the production of PCSK9. Inclisiran has been shown to be safe and only needs to be given by subcutaneous injection once every six months. It is expected to gain FDA approval soon.

**LE:** How long should someone take medications like these?

**Dr. Ozner:** Researchers have proposed that once early plaque is eliminated or advanced plaque is stabilized with aggressive LDL cholesterol lowering, to levels less than **40 mg/dL**,<sup>6,7</sup> the patient can then maintain an LDL cholesterol of **50 mg/dL to 70 mg/dL** with a healthy lifestyle and medications as needed to prevent future heart attacks or vascular events such as strokes.

If plaque recurs, then an intensive course of LDL cholesterol lowering can again be initiated.

There is also a “legacy” effect with cholesterol medications. In clinical trials with statin medications, it was noted that when the medication was stopped, there was a continued beneficial impact on heart disease risk for years.

We can therefore use aggressive cholesterol-lowering therapy to stabilize and shrink coronary plaques and then shift to lifestyle interventions and moderate medical therapy as needed thereafter to maintain LDL

cholesterol between **50 mg/dL** and **70 mg/dL** to achieve a significantly lower heart attack risk.

**LE:** We’ve talked a lot about cholesterol levels. Are there new medications that can dramatically lower triglyceride levels as well?

**Dr. Ozner:** Very high levels of triglycerides have also been a problem because they also increase heart attack risk. New medications are being developed (using a new technique called RNA therapeutics and gene silencing) that can lower triglyceride levels by **80%**.

In addition, a prescription-grade omega-3 fatty acid (icosapent ethyl or Vascepa®), which is an EPA-only fish oil has been approved by the FDA.

In the landmark REDUCE-IT trial,<sup>8</sup> this medication (**2 grams** twice a day) was used in patients at high cardiovascular risk who were already taking optimal statin therapy for LDL cholesterol control but had residual elevation of triglycerides. The net result was a highly significant lowering of major adverse cardiovascular events by **25%**.

Research has also shown that a high-quality fish oil supplement with both EPA and DHA can lower triglycerides.

**LE:** What blood tests do you recommend for uncovering hidden cardiovascular risk?

**Dr. Ozner:** I test my new patients by doing a complete blood count (CBC), chemistry panel, and standard lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides and non-HDL cholesterol). I also test for the number of







cholesterol-carrying particles (apolipoprotein B), high-sensitivity CRP (hs-CRP), and lipoprotein(a).

These tests are important for uncovering hidden risk for heart attack, stroke, and vascular disease, thereby allowing physicians to individualize treatment programs that will best lower their patients' risk of disability and death from cardiovascular disease.

**LE:** New medications appear to offer real hope for ending the heart disease epidemic.

**Dr. Ozner:** Indeed, we have turned the corner, as there is now sufficient research to conclude that cardiovascular disease (heart attack, stroke, and vascular disease) can be prevented and does not have to be the leading killer of men and women in the United States and worldwide.

With healthy lifestyle choices and new highly effective medications that are now available, we can reset our vascular aging clock and beat this formidable disease. We are at the dawn of a new era in cardiovascular medicine allowing us to achieve heart health and longevity. •

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

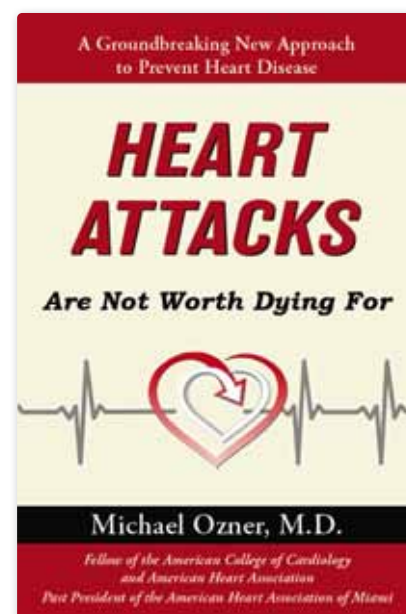
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Michael Ozner, MD, FACC, FAHA, is one of America's leading advocates for heart disease prevention. Dr. Ozner is a board-certified cardiologist, a Fellow of the American College of Cardiology and of the American Heart Association, Medical Director of Wellness & Prevention at Baptist Health South Florida and a well-known regional and national speaker in the field of preventive cardiology. He is a member of the *Life Extension®* Magazine Scientific Advisory Board. Dr. Ozner has frequently appeared in the print, radio and television media including *The New York Times*, *NPR* radio and *CBS News*. He was the recipient of the 2008 American Heart Association Humanitarian Award and has been elected to Top Cardiologists in America by the Consumer Council of America. Dr. Ozner is also the author of *The Great American Heart Hoax*, *Heart Attack Proof*, *The Complete Mediterranean Diet*, and his most recent book, *Heart Attacks Are Not Worth Dying For*.

To order a copy of *Heart Attacks Are Not Worth Dying For*, call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)

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# Lemon

BY LAURIE MATHENA



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Lemons are renowned for their tart flavor and fresh, clean scent.

Lemons may also help with weight loss. In one human study, pre-menopausal women with a high body mass index (BMI) followed a lemon detox diet for seven days. These women experienced greater improvements in insulin resistance, body fat, BMI, body weight, and waist-hip ratio than those on other diets.<sup>1</sup>

And a recent study published in the *European Journal of Nutrition* found that drinking acidic beverages like lemon juice with starchy food like bread could reduce their glycemic impact.<sup>2</sup> Specifically, the lemon juice lowered the mean blood glucose concentration peak by **30%** and delayed it more than **35 minutes**.

Lemon could also beneficially impact blood pressure, with one study showing that women who walked daily and consumed lemon juice had lower systolic blood pressure than those who didn't.<sup>3</sup>

And although there are no studies proving this, Ayurvedic medicine touts drinking lemon water in the morning to get your digestive system moving and prevent constipation.

Lemons are simple to incorporate throughout your day. You can squeeze fresh lemon juice onto fish or chicken dishes, add it to salads along with olive oil, or put it in a smoothie. Also consider adding lemon peels to drinking water for added flavor and nutrition.

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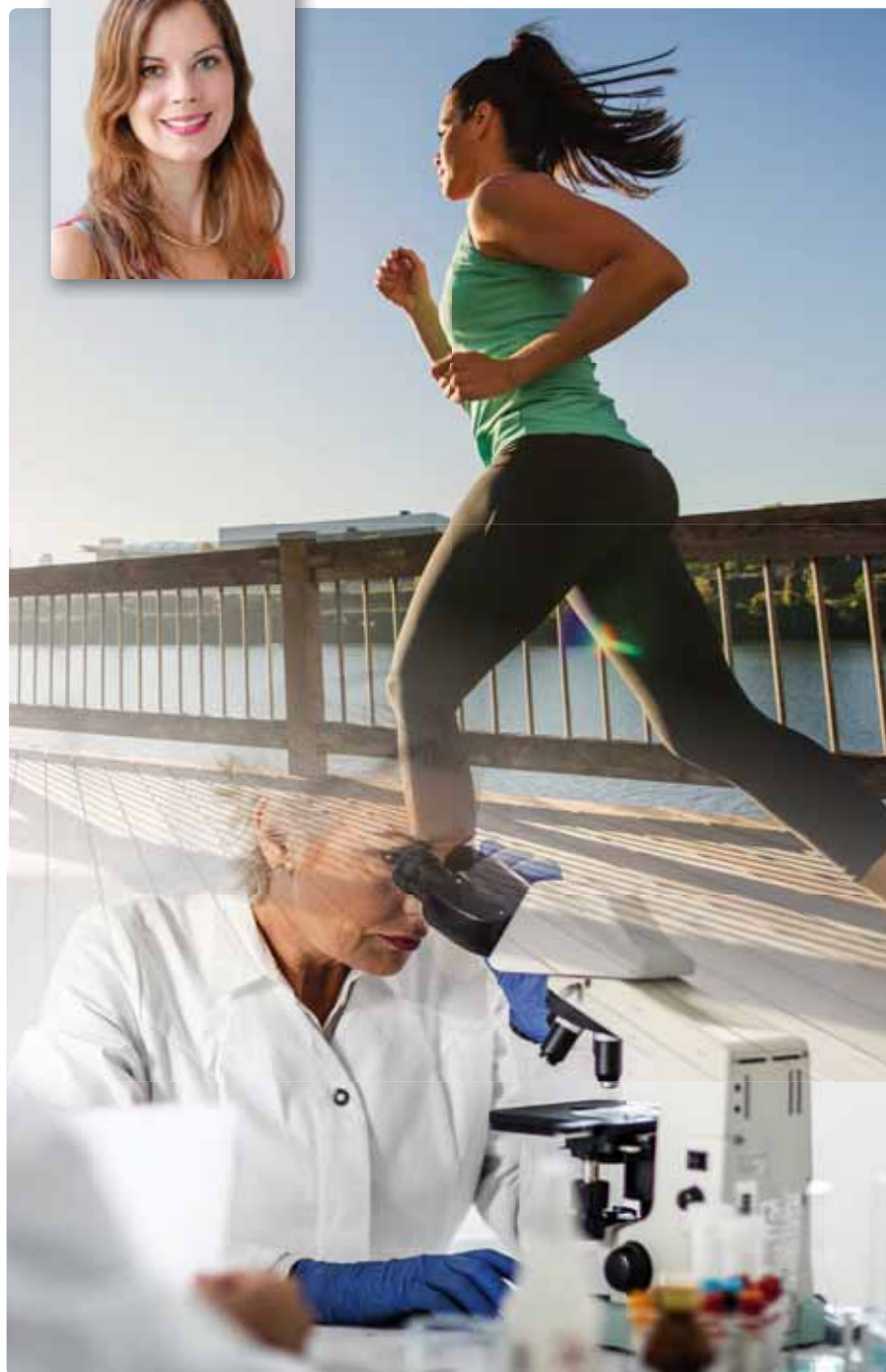
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# Vaginal Symptoms:

## Now an At-Home Test Can Identify Potential Causes and Treatments

DR. SHANTI ALBANI



**Vaginitis** or vaginal inflammation includes symptoms such as vaginal discomfort, itching, and discolored, malodorous discharge.

The most common causes are **yeast infections** and **bacterial vaginosis (BV)**, an overgrowth of harmful bacteria. These causes can be difficult to distinguish without laboratory testing.

**Life Extension®** now offers an at-home **Vaginosis Profile** test. In this interview, **Dr. Shanti Albani** explains how it can help women and their doctors determine the cause of their vaginal symptoms and identify treatment options.

**LE:** When would women need to use the **Vaginosis Profile**?

**Dr. Albani:** This test is meant for women who are experiencing vaginal discomfort or discharge. It can identify bacterial and yeast imbalances in their **vaginal flora** (the microorganisms that live in the vagina). That can help distinguish between a yeast infection and bacterial vaginosis.

**LE:** How is that helpful?

**Dr. Albani:** By profiling the vaginal flora, the **Vaginosis Profile** helps women and their practitioners identify vaginal microbiota problems. Then they can use a targeted approach to restore microflora harmony. It also identifies which treatments, either natural or pharmaceutical, are most likely to be effective. This is especially helpful for chronic and reoccurring vaginal infections, where organism resistance to prescriptive or natural agents causes persistent issues.

**LE:** Aren't most vaginal infections caused by yeast? If so, is there really a need for testing?

**Dr. Albani:** Contrary to widespread belief, the most common cause of vaginal symptoms is *not* yeast. It is **bacterial vaginosis**. Over-the-counter yeast treatments, such as Monistat®, will only be effective against yeast, not bacterial vaginosis.

**LE:** That's surprising. Can you tell us more about the differences between yeast infections and bacterial vaginosis?

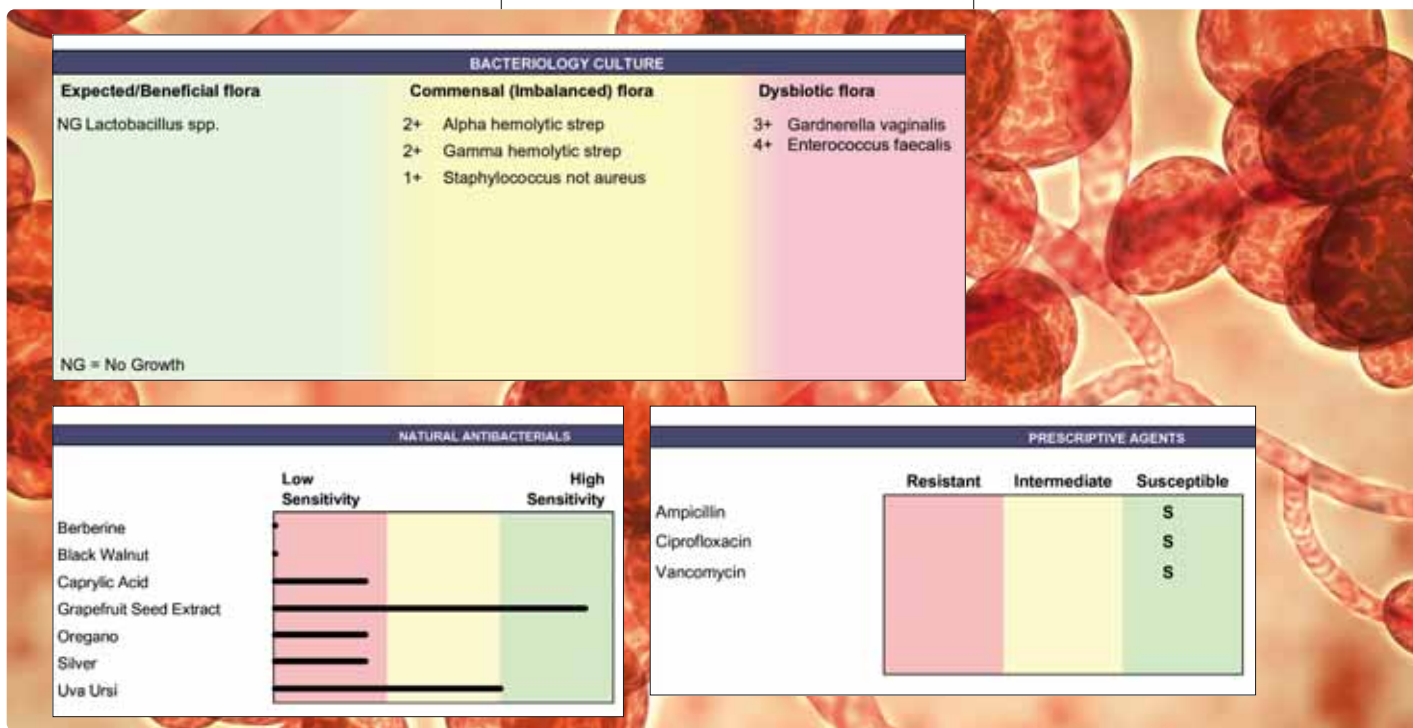
**Dr. Albani:** The most frequently implicated organism in vaginal **yeast infections** is *Candida albicans*, though other yeast species can be responsible. **Bacterial vaginosis**, on the other hand, occurs when anaerobic bacteria such as *Gardnerella vaginalis*, *Mycoplasma hominis*, or *Prevotella* increase and overcome the natural predominance of *Lactobacillus* bacteria. Included in this test is a yeast *and* bacterial culture, it can identify which species of yeast or bacteria may be causing symptoms. There are some symptoms that may correlate with a yeast versus bacterial vaginal infection, but the symptoms are not cut-and-dry. This test can help clarify and prevent misdiagnosis.

**LE:** After testing, is it simply a matter of discussing treatments with a physician?

**Dr. Albani:** Importantly, both bacterial vaginosis and yeast infections can develop resistance to antibiotic and antifungal medications. For this reason, the **Vaginosis Profile** includes **sensitivity testing**. This identifies the prescriptive and natural substances to which cultured microorganisms are susceptible or resistant. This takes much of the guesswork out of effective treatment, allowing a woman and her practitioner to target their approach.

**LE:** What else is included in the test?

**Dr. Albani:** Vaginal specimens are also carefully examined under the microscope for yeast, gram-negative bacteria, lactobacilli, red and white blood cells, eosinophils, and "**clue cells**." Clue cells are cells from the vagina that look fuzzy under the microscope. They take on this fuzzy appearance because they are coated with bacteria and their presence is one of the most specific confirmations of bacterial vaginosis.





The degree to which white blood cells are present helps evaluate the level of vaginal inflammation. Combined with the culture and sensitivity, the microscopic evaluation enhances the ability of the **Vaginosis Profile** to distinguish between bacterial vaginosis and yeast.

**LE:** How is the sample collected?

**Dr. Albani:** The test is an easy-to-use kit, allowing for self-collection in the comfort of your home. It includes a vaginal swab, which you use to gently collect a sample by rotating it for 15-30 seconds against the sides of the vagina. There's a collection tube into which the swab is placed for delivery to the lab. Once the collection is complete, it is sent to the lab using a provided pre-paid shipping label.

**LE:** Are there causes of vaginal discomfort that are *not* identified by the **Vaginosis Profile**?

**Dr. Albani:** The test differentiates between the two *most common* causes of vaginal symptoms, bacterial vaginosis and yeast infection, and looks at overall microflora imbalances. It can also indicate a possible allergic response if a specific type of white blood cell called **eosinophils** is elevated. However, it does not identify all causes of vaginitis. Some origins of vaginal discomfort not identified by the **Vaginosis Profile** include trauma, some skin conditions, and hormonal changes. This is also not a test for the sexually transmitted infections chlamydia, gonorrhea, or trichomonas. It is important that women discuss their symptoms and test results with their practitioners to ensure a more serious condition is not overlooked.



GRAM STAIN MICROSCOPY			
	Normal	Abnormal	Expected
Lactobacilli	<input type="checkbox"/>	None	Mod - Many
Curved Gram Negative Rods	<input type="checkbox"/>	Many	None
Small Gram Negative Rods	<input type="checkbox"/>	Many	None
Yeast	None	<input type="checkbox"/>	None
RBC's	None	<input type="checkbox"/>	None
WBC's	0	<input type="checkbox"/>	0 - 6
Clue Cells	<input type="checkbox"/>	Present	None
Eosinophils	N/A	<input type="checkbox"/>	None

Eosinophils reported and Wrights Stain performed when WBC's >6

**LE:** What else would you like women to know about the **Vaginosis Profile** and restoring vaginal health?

**Dr. Albani:** Since small numbers of yeast and anaerobic bacteria are part of a healthy vaginal flora, identifying what allowed these organisms to *overpopulate* is as important as proper diagnosis and treatment. Several culprits have been identified, including poor diet, poor hygiene, antibiotic use, hormonal changes, tight or damp clothes, corticosteroids, sexual contact, douching, underlying health conditions, and

use of chemical or scented hygiene products. Identifying underlying causes of flora imbalances allows women to make changes to optimize vaginal health and prevent reoccurrence.

**LE:** This sounds similar to a stool analysis test in the way it identifies problem microbes and flora imbalances. Is that accurate?

**Dr. Albani:** Yes. It is the same approach: testing for problematic microbes, assessing for microflora imbalances, and then using that

detailed information to restore balance and harmony. This **Vaginosis Profile** uses the same advanced technology used in stool testing to provide critical information about a woman's vaginal health. We now know that different areas of the body have differing microflora concentrations and that testing should be specific to the area in question. In the future you will see more body-specific areas of testing to assess microflora.

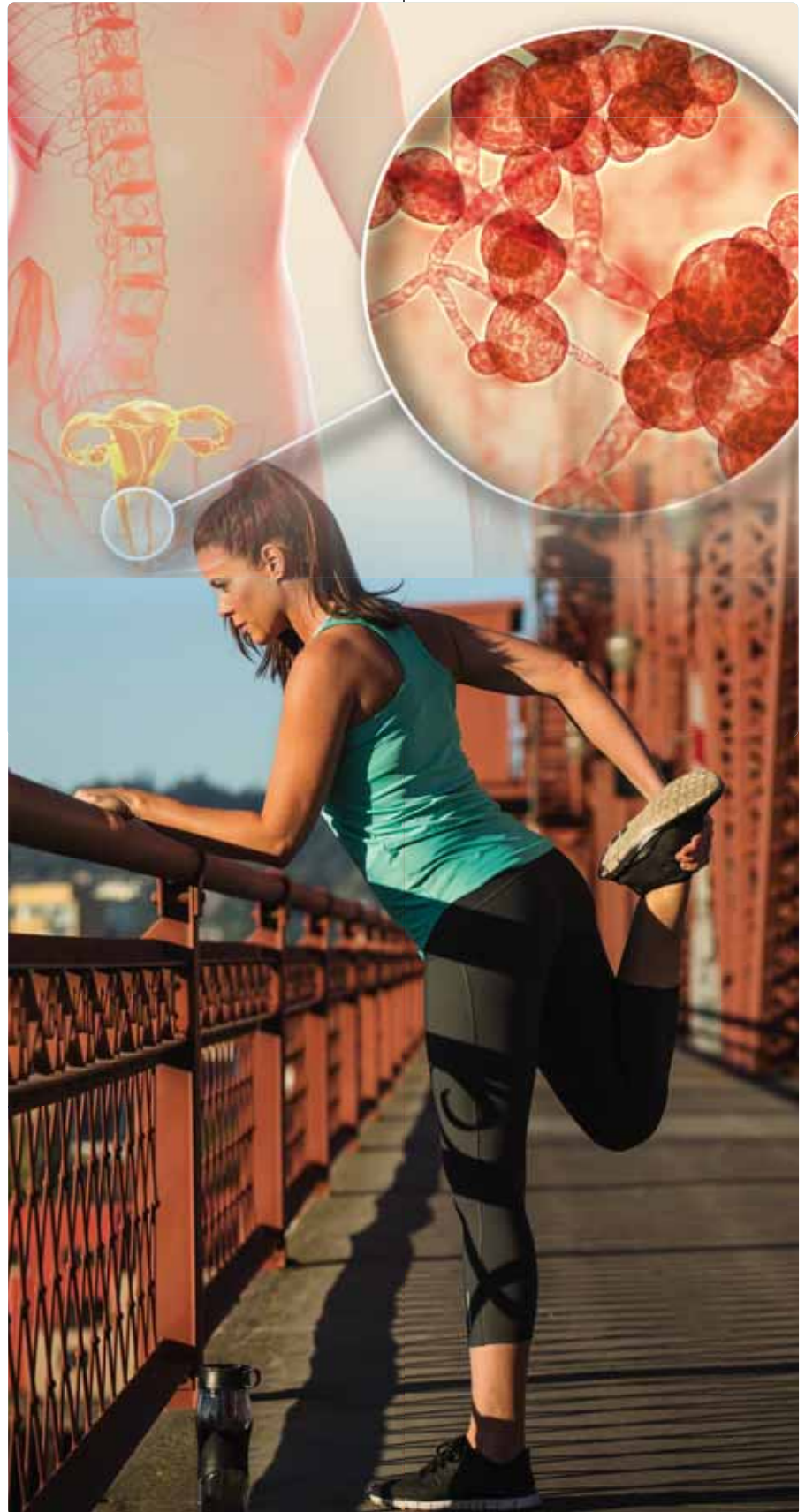
**LE:** Once someone has the test results, what are the next steps in using them to improve vaginal health?

**Dr. Albani:** All tests come with a detailed, written explanation of what the results may mean. That includes various treatment options. Customers can call in and speak with one of **Life Extension's** specially trained Wellness Specialists, who can discuss the meaning of the test results and suggest wellness options. Women should always work with their doctors, as well, to ensure proper treatment.

If you have any questions on the scientific content of this article, please call a **Life Extension®** Wellness Specialist at 1-866-864-3027.

**Dr. Shanti Albani** earned her medical degree in Naturopathic Medicine in 2003 from the National University of Natural Medicine in Portland, Oregon.

She practiced medicine for many years in central Mexico, specializing in gastrointestinal disorders and hormone balance. During this time she taught courses for physicians in bioidentical hormone replacement therapy. She has worked at **Life Extension®** since 2010 and is currently the Manager of Clinical Information.





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\*European Journal of Nutrition. 2011;50(5):387-389



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 02175 SAMe (S-Adenosyl-Methionine)  
 200 mg, 30 enteric coated vegetarian tablets  
 02176 SAMe (S-Adenosyl-Methionine)  
 400 mg, 30 enteric coated vegetarian tablets  
 02174 SAMe (S-Adenosyl-Methionine)  
 400 mg, 60 enteric coated vegetarian tablets

## MULTIVITAMINS

02199 Children's Formula Life Extension Mix™  
 02498 Comprehensive Nutrient Packs ADVANCED  
 02354 Life Extension Mix™ Capsules  
 02364 Life Extension Mix™ Capsules without Copper  
 02356 Life Extension Mix™ Powder  
 02355 Life Extension Mix™ Tablets  
 02357 Life Extension Mix™ Tablets with Extra Niacin  
 02365 Life Extension Mix™ Tablets without Copper  
 02292 Once-Daily Health Booster • 30 softgels  
 02291 Once-Daily Health Booster • 60 softgels  
 02313 One-Per-Day Tablets  
 02317 Two-Per-Day Capsules • 60 capsules  
 02314 Two-Per-Day Capsules • 120 capsules  
 02316 Two-Per-Day Tablets • 60 tablets  
 02315 Two-Per-Day Tablets • 120 tablets

## NERVE & COMFORT SUPPORT

02202 ComfortMAX™  
 02303 PEA Discomfort Relief

## PERSONAL CARE

01006 Biosil™ • 5 mg, 30 veg capsules  
 01007 Biosil™ • 1 fl oz  
 00321 Dr. Proctor's Advanced Hair Formula  
 00320 Dr. Proctor's Shampoo  
 02322 Hair, Skin & Nails Collagen Plus Formula  
 01278 Life Extension Toothpaste  
 00408 Venotone  
 00409 Xyliwhite Mouthwash  
 02304 Youthful Collagen  
 02252 Youthful Legs

## PET CARE

01932 Cat Mix  
 01931 Dog Mix

## PROBIOTICS

01622 Bifido GI Balance  
 01825 FLORASSIST® Balance  
 02125 FLORASSIST® GI with Phage Technology  
 01821 FLORASSIST® Heart Health  
 02250 FLORASSIST® Mood Improve  
 02208 FLORASSIST® Immune & Nasal Defense  
 02120 FLORASSIST® Oral Hygiene  
 02203 FLORASSIST® Prebiotic  
 01920 FLORASSIST® Throat Health  
 02400 FLORASSIST® Winter Immune Support  
 52142 Jarro-Dophilus® for Women  
 00056 Jarro-Dophilus EPS® • 60 veg capsules  
 21201 Jarro-Dophilus EPS® • 120 veg capsules  
 01038 Theralac® Probiotics  
 01389 TruFlora® Probiotics

## SKIN CARE

80157 Advanced Anti-Glycation Peptide Serum  
 80165 Advanced Growth Factor Serum  
 80170 Advanced Hyaluronic Acid Serum  
 80154 Advanced Lightening Cream  
 80155 Advanced Peptide Hand Therapy  
 80175 Advanced Probiotic-Fermented Eye Serum  
 80177 Advanced Retinol Serum  
 80152 Advanced Triple Peptide Serum  
 80140 Advanced Under Eye Serum with Stem Cells  
 80137 All-Purpose Soothing Relief Cream  
 80139 Amber Self MicroDermAbrasion  
 80118 Anti-Aging Mask  
 80151 Anti-Aging Rejuvenating Face Cream  
 80153 Anti-Aging Rejuvenating Scalp Serum  
 80179 Brightening Peptide Serum  
 80176 Collagen Boosting Peptide Cream



80156 Collagen Boosting Peptide Serum  
 02408 Collagen Peptides for Skin & Joints  
 80169 Cucumber Hydra Peptide Eye Cream  
 02423 Daily Skin Defense  
 80141 DNA Support Cream  
 80163 Eye Lift Cream  
 80123 Face Rejuvenating Anti-Oxidant Cream  
 80109 Hyaluronic Facial Moisturizer  
 80110 Hyaluronic Oil-Free Facial Moisturizer  
 80138 Hydrating Anti-Oxidant Facial Mist  
 00661 Hydroderm  
 55495 Instensive Moisturizing Cream  
 80103 Lifting & Tightening Complex  
 80168 Melatonin Advanced Peptide Cream  
 80114 Mild Facial Cleanser  
 80172 Multi Stem Cell Hydration Cream  
 80159 Multi Stem Cell Skin Tightening Complex  
 80122 Neck Rejuvenating Anti-Oxidant Cream  
 80174 Purifying Facial Mask  
 80150 Renewing Eye Cream  
 80142 Resveratrol Anti-Oxidant Serum  
 01938 Shade Factor™  
 02129 Skin Care Collection Anti-Aging Serum  
 02130 Skin Care Collection Day Cream  
 02131 Skin Care Collection Night Cream  
 80166 Skin Firming Complex  
 02096 Skin Restoring Ceramides  
 80130 Skin Stem Cell Serum  
 80164 Skin Tone Equalizer  
 80143 Stem Cell Cream with Alpine Rose  
 80148 Tightening & Firming Neck Cream  
 80161 Triple-Action Vitamin C Cream  
 80162 Ultimate MicroDermabrasion  
 80173 Ultimate Peptide Serum  
 80178 Ultimate Telomere Cream  
 80160 Ultra Eyelash Booster  
 80101 Ultra Wrinkle Relaxer  
 80113 Under Eye Refining Serum  
 80104 Under Eye Rescue Cream  
 80171 Vitamin C Lip Rejuvenator  
 80129 Vitamin C Serum  
 80136 Vitamin D Lotion  
 80102 Vitamin K Cream

## SLEEP

01512 Bioactive Milk Peptides  
 02300 Circadian Sleep  
 01551 Enhanced Sleep with Melatonin  
 01511 Enhanced Sleep without Melatonin  
 02234 Fast-Acting Liquid Melatonin  
 01669 Glycine  
 02308 Herbal Sleep PM  
 01722 L-Tryptophan  
 01668 Melatonin • 300 mcg, 100 veg capsules  
 01083 Melatonin • 500 mcg, 200 veg capsules  
 00329 Melatonin • 1 mg, 60 capsules  
 00330 Melatonin • 3 mg, 60 veg capsules  
 00331 Melatonin • 10 mg, 60 veg capsules  
 00332 Melatonin • 3 mg, 60 veg lozenges  
 02201 Melatonin IR/XR  
 01787 Melatonin 6 Hour Timed Release  
 300 mcg, 100 veg tablets  
 01788 Melatonin 6 Hour Timed Release  
 750 mcg, 60 veg tablets  
 01786 Melatonin 6 Hour Timed Release 3 mg, 60 veg tablets  
 01721 Optimized Tryptophan Plus  
 01444 Quiet Sleep  
 01445 Quiet Sleep Melatonin

## VITAMINS

01533 Ascorbyl Palmitate  
 00920 Benfotiamine with Thiamine  
 00664 Beta-Carotene  
 01945 BioActive Complete B-Complex  
 00102 Biotin  
 00084 Buffered Vitamin C Powder  
 02229 Fast-C® and Bio-Quercetin Phytosome  
 02075 Gamma E Mixed Tocopherol Enhanced with  
 Sesame Lignans  
 02070 Gamma E Mixed Tocopherol & Tocotrienols  
 01913 High Potency Optimized Folate  
 01674 Inositol Caps  
 02244 Liquid Vitamin D3 • 50 mcg (2000 IU)  
 02232 Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)  
 01936 Low-Dose Vitamin K2  
 00065 MK-7  
 00373 No Flush Niacin  
 01939 Optimized Folate (L-Methylfolate)  
 01217 Pyridoxal 5'-Phosphate Caps  
 01400 Super Absorbable Tocotrienols  
 02334 Super K  
 02335 Super K Elite  
 01863 Super Vitamin E  
 02028 Vitamin B5 (Pantothenic Acid)  
 01535 Vitamin B6  
 00361 Vitamin B12 Methylcobalamin  
 01536 Vitamin B12 Methylcobalamin • 1 mg, 60 veg lozenges  
 01537 Vitamin B12 Methylcobalamin • 5 mg, 60 veg lozenges  
 02228 Vitamin C and Bio-Quercetin Phytosome  
 1,000 mg, 60 veg tablets  
 02227 Vitamin C and Bio-Quercetin Phytosome  
 1,000 mg, 250 veg tablets  
 01753 Vitamin D3 • 25 mcg (1000 IU), 90 softgels  
 01751 Vitamin D3 • 25 mcg (1000 IU), 250 softgels  
 01713 Vitamin D3 • 125 mcg (5000 IU), 60 softgels  
 01718 Vitamin D3 • 175 mcg (7000 IU), 60 softgels  
 01758 Vitamin D3 with Sea-Iodine™  
 02040 Vitamins D and K with Sea-Iodine™

## WEIGHT MANAGEMENT & BODY COMPOSITION

00658 7-Keto® DHEA Metabolite • 25 mg, 100 capsules  
 02479 7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules  
 01509 Advanced Anti-Adipocyte Formula  
 01807 Advanced Appetite Suppress  
 02207 AMPK Metabolic Activator  
 01492 Calorie Control Complex with Phase 3™ and  
 African Mango  
 02478 DHEA Complete  
 01738 Garcinia HCA  
 01292 Integra-Lean®  
 01908 Mediterranean Trim with Sinetrol™ -XPur  
 01432 Optimized Saffron  
 00818 Super CLA Blend with Sesame Lignans  
 01902 Waist-Line Control™  
 02151 Wellness Code® Appetite Control

## WOMEN'S HEALTH

01942 Breast Health Formula  
 01626 Enhanced Sex for Women 50+  
 01894 Estrogen for Women  
 01064 Femmenessence MacaPause®  
 02204 Menopause 731™  
 02319 Prenatal Advantage  
 01441 Progesta-Care®  
 01649 Super-Absorbable Soy Isoflavones

# 'C'

## TO THE MAX

Humans don't manufacture **vitamin C** internally, so it must be obtained through dietary sources or supplements.

**Vitamin C** is water soluble and needs to be constantly replenished.\*

A highly *absorbable* form of **quercetin** complements vitamin C's activity in the body.

Each tablet provides **1,000 mg** of vitamin C and **15 mg** of Bio-Quercetin Phytosome.

**Item #02227 • 250 vegetarian tablets**

1 bottle **\$22.50** • 4 bottles \$20 each



For full product description and to order **Vitamin C and Bio-Quercetin Phytosome**, call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)

\* PLoS Med. 2005 Sep;2(9):e307;author reply e309.



These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.



# FORESIGHT FOR YOUR EYESIGHT

## MacuGuard® Ocular Support with Saffron & Astaxanthin provides:

1. Lutein, *trans*-zeaxanthin, and meso-zeaxanthin to help maintain structural integrity of the macula and retina.<sup>1-5</sup>
2. Alpha-carotene to further help support macular density.<sup>1</sup>
3. Cyanidin-3-glucoside to assist with night vision.<sup>6-8</sup>
4. Astaxanthin for comprehensive eye health support and to fight eye fatigue.<sup>9</sup>
5. Saffron to help support vision, based on study subjects seeing an average of two additional lines on eye chart used by doctors to test vision.<sup>1</sup>

Also available: MacuGuard® Ocular Support with Saffron. Does not contain Astaxanthin.

#### References

1. JAMA Ophthalmol. 2015;133(12):1415-24.
2. Nutrients. 2013 April;5(4):1169-85.
3. Nutrition. 2011 Sep;27(9):960-6.
4. Free Radic Biol Med. 2012;53(6):1298-307.
5. J Ophthalmol. 2015;2015:523027.
6. Evid Based Complement Alternat Med. 2012;2012:429124.
7. Invest Ophthalmol Vis Sci. 2010;51(12):6118-24.
8. J Agric Food Chem. 2003 Jun 4;51(12):3560-3.
9. Altern Med Rev. 2011 Dec;16(4):355-64.

For full product description and to order MacuGuard® Ocular Support with Saffron or MacuGuard® Ocular Support with Saffron & Astaxanthin, call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)



#### MacuGuard® Ocular Support with Saffron

Item #01992 • 60 softgels

1 bottle \$18.75 • 4 bottles \$17.50 each



#### MacuGuard® Ocular Support with Saffron & Astaxanthin

Item #01993 • 60 softgels

1 bottle \$33 • 4 bottles \$30 each

Each bottle lasts for two months.

LuteinPlus® and Mz® are registered trademarks of NutriProducts Ltd., UK, licensed under U.S. Patent 8,623,428.

These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.





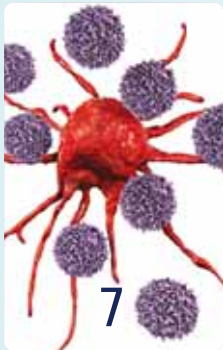
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**Advanced-stage prostate cancer** cases are increasing due to a flawed government recommendation for men to avoid PSA screening.



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